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# **PHALANGEAL FRACTURES: CURRENT TREATMENTS, COMPLICATIONS AND INNOVATIONS**

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PHALANGEAL FRACTURES:  
CURRENT TREATMENTS, COMPLICATIONS AND INNOVATIONS  
THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To Fredrik



## ABSTRACT

Phalangeal fractures are common and most of them heal well without surgical intervention. However, the comminuted and displaced unstable fractures sometimes require surgery. There are many different surgical options available such as K-wires, screws of different kinds, plates and screws, and external fixations. The outcome varies widely in the literature when it comes to results and complications caused by the different osteosynthesis methods. The aims of this thesis are to:

1. Analyze the practice in our department regarding surgery of phalangeal finger fractures including choice of surgical method, complications and reoperations.
2. Investigate the properties of and participate in the development of a new method of fracture fixation- an adhesive suited for bone repair.
3. Examine the potential benefit of adhesion barriers in fracture treatment.

In Paper I patient files of all patients treated surgically for a closed intraarticular fracture of the base or middle phalanx of the fingers during the period from 2010-2014 at the Department of Hand Surgery at Södersjukhuset were examined retrospectively. Fracture type, operation method and reoperations were analyzed. Results showed a higher incidence of reoperations due to adhesions and resulting finger stiffness in patients operated with a plate than when K-wires or screws only were used. When adjusting for fracture complexity, the results were no longer significant indicating that a more complex fracture in itself also causes more adhesions and finger stiffness and leads to more reoperations than the less complicated ones.

In Paper II, a thiol-ene composite, which is a new material being investigated for bone repair, was tested biomechanically and biologically in a rat femur fracture model. The composite shows good stability both *ex vivo* in a fatigue model, and after five weeks *in vivo*. There were no signs of reduced bone healing in presence of the new material, no signs of inflammation, and it had maintained 60% of its adhesion strength to bone after 5 weeks *in vivo*.

In Paper III, the effects of the adhesion barrier Dynavisc® was evaluated in a pilot study of 10 patients as a first step of a planned randomized controlled trial. The adhesion barrier was applied during surgery after fixation of fractures or osteotomies of extraarticular base phalanges with plates and screws. Finger total active motion (TAM) was evaluated after three months and one year and compared to the TAM of the contralateral finger. Only two patients reached the hypothesized result of a difference of less than 20 degrees of TAM to the contralateral finger.

Paper IV is a study of a further development of the thiol-ene composite studied in Paper II, now used as an adhesion barrier called DendroPrime. 12 rabbits were operated on the second toe of the hind paws. A plate was attached to the plantar side of the base phalanx with two screws, after scratching the periosteum inducing a trauma to the bone. On one side the plate was coated with DendroPrime, on the other paw it was left bare. After seven weeks the mobility of the toe was examined in a biomechanical testing device by pulling the tendons with forces from 0 N to 5 N. There was significantly better mobility in toes treated with DendroPrime than in toes with a bare plate at forces of 1 N, 3 N, 4 N and 5 N. The results indicate a potential benefit of this material to reduce complications related to adhesions after fracture surgery.

## LIST OF SCIENTIFIC PAPERS

- I. Reoperations and postoperative complications after osteosynthesis of phalangeal fractures: a retrospective cohort study. von Kieseritzky J, Nordström J, Arner M. J Plast Surg Hand Surg 2017 Dec;51(6):458-462.
- II. High-performance thiol-ene composites unveil a new era of adhesives suited for bone repair. Granskog V, García-Gallego S, von Kieseritzky J, Rosendahl J, Stenlund P, Zhang Y, Petronis S, Lyvén B, Arner M, Håkansson J, Malkoch M. Adv Funct Mater 2018; 28:10.
- III. Dynavisc® as an adhesion barrier in finger phalangeal plate fixation – a pilot study of ten patients. von Kieseritzky J, Rosengren J, Arner M Submitted manuscript.
- IV. DendroPrime as an adhesion barrier in fracture surgery – an experimental study in rabbits. von Kieseritzky J, Alfort H, Granskog V, Hutchinson D, Stenlund P, Bogestål Y, Arner M Håkansson J, Malkoch M. Submitted manuscript.



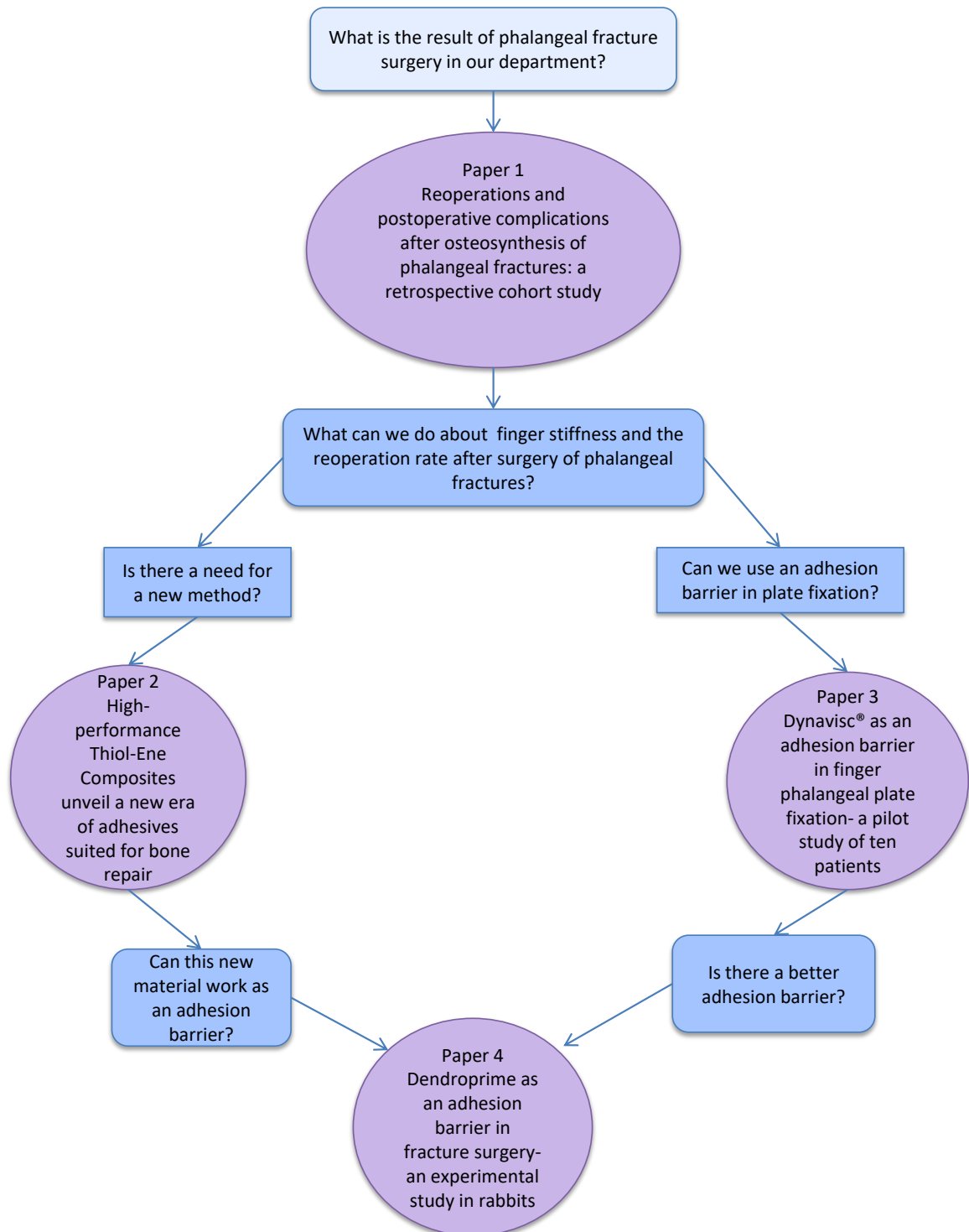
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## LIST OF ABBREVIATIONS

AO	Arbeitsgemeinschaft für Osteosynthesfragen. A non-profit global network for surgical treatment of trauma.
BAPA	2,2-Bis-(alloxymethyl)propionic acid
BMD	Bone Mineral Density
BV	Bone Volume
CE	Conformité Européenne. Certification mark on medical devices required for trade in the EU.
CMC	Carboxymethylcellulose
DIP joint	Distal interphalangeal joint
DOPA	3,4- Dihydroxyphenylalanine
ETTTP	Ethoxylated trimethylolpropane tri (3-mercapto-propionate)
FESSH	Federation of European Societies for Surgery of the Hand
FDP	Flexor Digitorum Superficialis
FDS	Flexor Digitorum Profundus
FRAP	Fiber Reinforced Adhesive Patch
GLP	Good Laboratory Practice
GRF	Gelatin Resorcinol Formol
HEV light	High Energy Visual light
K-wires	Kirschner wires
MAP	Mussel Adhesive Protein
MCP joint	Metacarpophalangeal joint
N	Newton, SI-unit for force
ORIF	Open Reduction and Internal Fixation
PEG	Polyethylene glycol
PET	Polyethyleneterephthalate
PFA	Paraformaldehyde
PIP joint	Proximal interphalangeal joint
PMMA	Poly(methyl methacrylate)
RCT	Randomized Controlled Trial
RISE	Research Institutes of Sweden AB
TAM	Total Active Motion
TATATO	1,3,5-Triallyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione
TEC	Thiol-Ene Coupling
TEMPIC	Tris[2-(3-mercapto propionyloxy)ethyl]isocyanurate
TV	Tissue Volume

# THESIS FLOW CHART





# PHALANGEAL FRACTURES OF THE FINGERS

## BACKGROUND

Phalangeal fractures of the fingers are common. In the upper extremity, phalangeal fractures of the fingers are the second most common fractures after fractures of the radius and ulna (Karl et al. 2015). The injuries affect all ages but most patients are of working age resulting in high cost for the health care system as well as secondary costs to society related to sick leave during healing and rehabilitation (de Putter et al. 2012; Rosberg et al. 2005; Rosberg and Dahlin 2004; van Onselen et al. 2003).

Distal phalangeal fractures are often open injuries caused by crush trauma or amputation. Associated injuries to the nail bed and matrix are common. Soft tissue damage and nail injuries are often extensive. Closed fractures of the distal phalanx can occur after compression trauma and hyperflexion trauma and are frequent in ball sports. The common mallet fracture is an avulsion of the bony insertion of the extensor tendon. Nail and nail bed are important structures when treating fractures of the distal phalanx (Carpenter and Rohde 2013). This thesis is predominantly oriented towards fractures of the proximal and middle phalanx and therefore distal phalangeal fractures will not be addressed further.

Middle and proximal phalanx fractures can be divided into groups depending on the location on the phalanx: intraarticular or extraarticular, in the base, the diaphysis or distal. Wherever they are located they have one thing in common- they all affect the mobilization of the proximal interphalangeal joint (PIP) which is crucial for finger- and hand function (Bhatt et al. 2014). Open injuries of the middle and proximal phalanx are often associated with tendon and nerve injuries. A common mechanism of injury is machine accidents which more often occurs in men (De Jonge et al. 1994).

Evidence based guidelines for treatment of phalangeal fractures are lacking due to often contradictory results from different studies. Most uncomplicated, stable fractures that do not affect joint surfaces or give a malalignment to the finger can be treated conservatively with cast or buddy tape (Giddins 2015). In case of considerable malalignment, the fracture is unstable, or a joint surface is significantly affected, surgical intervention can be indicated. There is a wide variety of treatment options, including closed or open reduction and K-wire fixation, open reduction and internal fixation (ORIF) with screws or screws and plate, intraosseous wiring, intramedullary screws, static or dynamic external fixation, and various combinations of the aforementioned (Black et al. 1986; Carpenter and Rohde 2013; Fyfe and Mason 1979). All methods have their advantages and disadvantages, and there is no consistent evidence that one method would be generally superior to the other. Comparison between studies is difficult due to complexities in the different studies with regard to fracture type, fracture localization, open or closed injuries, rehabilitation regimes, timing of evaluation, associated soft tissue injuries etc. The fracture pattern itself is considered important for the choice of treatment. A spiral fracture, for instance, has completely different treatment options compared to a transverse fracture or a comminuted fracture (Carpenter and Rohde 2013; Markiewicz 2013). The uniqueness of every fracture makes it hard to draw general conclusions from previous research.

One of the most common complications after phalangeal fracture treatment is finger joint stiffness. This applies both for fractures treated conservatively as well as for operated fractures. The stiffness is a result of adhesions between bone and tendons and between tendons and skin due to finger immobilization or scar tissue caused by

surgery (Barton 1984). A persisting deformity of the bone because of insufficient fracture reduction is another cause of stiffness that often results in PIP joint extension lag (Freeland et al. 2003; Page and Stern 1998). Associated joint involvement, tendon injuries, skin loss or more than one fracture on the same finger contributes to stiffness, even in uninjured fingers in the same hand (Huffaker et al. 1979).

Despite the many surgical treatment options available, highly comminuted fractures where the fragments are too small for screws or K-wires, remain highly challenging for surgeons. One innovative idea would involve fixation of small fracture fragments with a surgical glue. Currently, however, there is no such glue available on the market with an adhesion strength good enough for fracture fixation in a wet environment (Farrar 2012).

## **EPIDEMIOLOGY**

In a Dutch study running over 23 years, the incidence of phalangeal fractures was 2.9%. The incidence for men was 3.2% compared with women at 2.4% (De Jonge et al. 1994). In a study based on a registered population of 87 million Americans the incidence was described as 12.5 per 10000 person years (Karl et al. 2015). Another Dutch study based on the patients from an emergency department in Amsterdam found that 59% of all hand fractures affected the phalanges. In that study the distribution showed equal numbers of distal and proximal phalanx fractures (38% each), while middle phalanx fractures were less common (22%) (van Onselen et al. 2003). In a Norwegian study, 46% of the hand fractures were phalangeal fractures (Hove 1993) and in an American study 23% of all hand and forearm fractures were phalangeal fractures (Chung and Spilson 2001).

Sex and gender distribution show that men are more likely to get a phalangeal fracture during adolescence and adulthood while women are more likely to fracture their fingers after retirement (De Jonge et al. 1994; van Onselen et al. 2003).

## **TREATMENT METHODS**

### **CONSERVATIVE TREATMENT**

In the beginning of the 20<sup>th</sup> century non-operative treatment was the most common option for phalangeal fractures, and is still an excellent choice in most cases (Giddins 2015; Singh et al. 2011). According to Barton as many as 75% of all finger fractures can be treated conservatively (Barton 1984). This has also been shown in unstable cases (Held et al. 2013). The first challenge is to determine if the fracture is suitable for conservative treatment and if it is dislocated, reduce it. The second challenge is to fix it in a good cast, splint or buddy tape, and the third challenge is to start mobilization in time. Therefore, conservative treatment is no easy choice. It requires frequent follow-up, re-evaluation, and modification of splints and mobilization (Giddins 2015). Reducing a fracture during the first few days after the trauma is usually straightforward, while a malunion may require corrective osteotomy which can be very demanding and time consuming. The choice of immobilization technique also requires thorough consideration; questions that need to be answered are whether the fracture is stable enough for buddy taping, and if not, what kind of cast or splint that is the best? The minimum immobilization time needed to provide enough stability for active motion exercises without risking dislocation must also be assessed. (Barton 1984). It is important to remember that conservative treatment is, or at least should be, an active treatment (Giddins 2015). Another consideration is

how many adjacent joints to include in the cast or splint. For proximal phalangeal fractures for instance, there was no difference in outcome using the Lucerne cast, where the wrist is free during the cast treatment compared to a long conventional cast in which the wrist is not free. However, wrist motion at the end of treatment was better in patients treated with the Lucerne cast (Franz et al. 2012). If instability of the fracture requires total immobilization in a cast, the safe position of the hand with flexed MCP joints and straight PIP and DIP joints is considered optimal (James 1970; Wright 1968) (Figure 1). The advantage of this position is based upon the anatomy of the collateral ligaments of the finger joints (Kuczynski 1968).

Immobilization time cannot exceed four weeks or joint stiffness will reduce hand function. This has been demonstrated by Wright in his work from 1968 where he showed that immobilization resulted in deterioration of function week by week where four weeks was a breaking point (Wright 1968).



*Figure 1. Safe position in cast fixation.*

## **SURGICAL TREATMENT**

### **Kirschner wire fixation**

Kirschner-wire (K-wire) fixation is an old and well proven method that has shown excellent results in several studies both for transverse and spiral fractures (Belsky et al. 1984; Eberlin et al. 2014; Egloff et al. 2012; Shewring et al. 2018). Other studies have conversely shown an increase in complications in K-wire fixation compared to other methods in terms of finger stiffness, need for reoperation and additional complications due to superficial infections around the wire ends (El-Saeed et al. 2019; Faruqui et al. 2012; Hsu et al. 2011; Pun et al. 1989).

The goal of K-wire fixation is to reduce malalignment and supply enough stability to mobilize earlier than in conservative treatment without locking soft tissues with the wires. Closed reduction and percutaneous K-wire fixation is a technique requiring radiographs in two projections and an awareness of where the safe entry points for the pins are located (Rex et al. 2015) (Figure 2). Failure to get the wires in the right position may result in insufficient stability. K-wires that catch soft tissues might block the joint mobility that was the goal of the treatment (Rex et al. 2015; Saied and Sabet Jahromi 2018). Successful pinning of fractures is very much a question of training and three-dimensional visualization. To gain the required stability one must place the correct number of K-wires of optimal size in the correct position (Black et al. 1986; Fyfe and Mason 1979; Massengill et al. 1982; Massengill et al. 1979; Vanik et al. 1984). For extra stability K-wire fixation can be combined with open methods, but this means open surgery and the associated disadvantages of soft tissue scarring. The combination with wiring has shown great stability, as is the case, for example, with theta fixation (Gould et al. 1984; Thomas et al. 2015). Despite a rapid development of new techniques for fracture fixation of fingers, K-wires remain a work-horse for many surgeons and perform well in several studies when compared with ORIF (Egloff et al. 2012; Kose et al. 2018; Pandey et al. 2018; Reformat et al. 2018; Shewring et al. 2018; Takigami et al. 2010). Aesthetic outcome is also appreciated by patients treated with K-wires compared to other methods (Kootstra et al. 2019)



*Figure 2. K-wire fixation for subcapitular fracture of the middle phalanx provides enough stabilization for early mobilization of the PIP joint.*

### **Screw fixation**

Screw fixation of a phalangeal fracture, using cortical screws alone, is only possible in long oblique or spiral fractures where the length of the fracture line equals at least two times the width of the phalanx (Kozin et al. 2000). The standard procedure in this case is to place two screws, after minimal soft tissue dissection, in a straight angle to the fracture line and to use lag-technique for compression (Figure 3). The screw heads should be put deep into the cortex of the bone in order to avoid disturbing soft tissues. This will give a stable fixation that allows for early mobilization

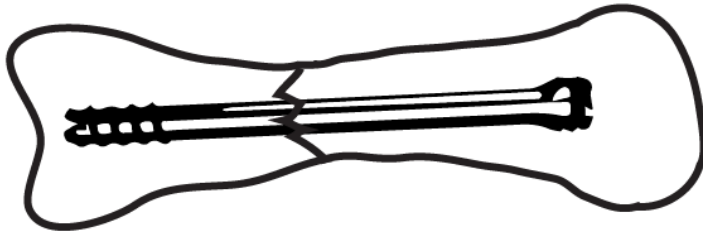


and is a good choice for this kind of fracture in a finger phalanx (Başar et al. 2015; Black et al. 1986; Egloff et al. 2012). Inserting more than two lag-screws does not contribute to extra stability and will only prolong operation time and increase the cost (Zelken et al. 2015). A more modern version of screw treatment is to use percutaneous headless cannulated compression screws in the same manner as described above. In this case the procedure can be performed completely percutaneously, which saves the soft tissues and prevents adhesion formation and finger stiffness. Excellent results have been reported using this technique (Liodaki et al. 2017).



*Figure 3. Lag screw fixation of a spiral fracture of the proximal phalanx.*

Intramedullary headless cannulated screws are the latest contribution to screw fixation of phalanges. A K-wire is inserted percutaneously through the joint surface of the MCP or the PIP joint depending on the fracture. The cannulated screw is inserted over the K-wire which is then removed when the screw is in place (Figure 4). The screw provides a very rigid fixation with compression, soft tissue irritation is minimal, and early mobilization is started (del Pinal et al. 2015; Giesen et al. 2016; Jovanovic et al. 2018). This fixation is very stable and has even exceeded the strength of plate fixation in experimental models (Borbas et al. 2016; Ibanez et al. 2015). Patients operated with this technique return to work and normal daily activities faster than patients operated with other techniques (Esteban-Feliu et al. 2019). So far there have been no reports of complications due to the entry through the joint surface. The damage to the cartilage is limited to only 4% of the cartilage surface of the base of the proximal phalanx when using 2.2 mm screws (Borbas et al. 2016), however one must keep in mind that there is no long-term follow-up on this technique available yet. The technique is not recommended for comminute and unstable fractures which cannot tolerate the compression (del Pinal et al. 2015).



*Figure 4. Schematic intramedullary headless screw fixation.*

### **Fixation with plates and screws**

The advantage of plate fixation is that it provides a good stability even in very comminuted and unstable fractures (Massengill et al. 1982) (Figure 5). Depending on the fracture, plates can be used either as a sole treatment or in addition to screws and K-wires, providing increased stability. Plate fixation is often only recommended for comminuted unstable fractures (Henry 2008). The evolution of product development of plates for finger fractures has resulted in thinner plates designed to fit all kinds of fractures, and systems are currently available in both steel and titanium. Locking plates and screws for hand fractures have also reached the market, enabling a solid fixation using monocortical screws (Doht et al. 2014; Shanmugam et al. 2015).

Despite this development, interference with soft tissue, especially the extensor tendon over the proximal phalanx, is inevitable (Nunley and Kloen 1991). Adhesions in this area are common after plate fixation and cause stiffness especially of the PIP-joint (Onishi et al. 2015). Factors described to influence the results are the condition of the soft tissue, joint involvement, fracture location and characteristics and perhaps most importantly, plate placement (Chow et al. 1991; Ouellette et al. 2004). The dorsal tendon splitting technique provides a good exposure of the fracture (Pratt 1959), whereas the lateral approach is claimed to cause less adhesions but is more technically demanding (Freeland et al. 2001).

There are many studies that report on outcome after the use of plate and screws on phalangeal fractures and the results vary considerably. Excellent results have been reported on lateral plate placement where one lateral band has been removed (Bannasch et al. 2010; Bosscha and Snellen 1993; Dabezies and Schutte 1986). However, in the cases of Bosscha and Snellen and Bannasch metacarpal fractures were also included in the studies, making comparison difficult. Metacarpal fractures are not as problematic as proximal phalangeal fractures concerning closeness to the extensor mechanism and have no association to the PIP joint as phalangeal fractures do. Other authors have reported considerable problems after plate fixation in terms of adhesions, and consequently, finger stiffness, despite lateral plate placement (Pun et al. 1991). Robinson and co-workers on the other hand could not see any difference in outcome related to plate placement (Robinson et al. 2017), but this in turn is contradicted by Onishi et al, who could show that dorsal plate placement was a predictor for a bad outcome regarding joint motion (Onishi et al. 2015). Other complications, in addition to finger stiffness, such as infection and tendon rupture, have also been reported (Page and Stern 1998; Stern et al. 1987). New and modern plates do not seem to improve the results regarding finger stiffness. In the Brei-Thoma study from 2015, 12 out of 32 patients required secondary procedures, including plate removal and correction osteotomies, and 67%

of the patients had an extension lag of the PIP joint (Brei-Thoma et al. 2015). High reoperation rate after plate fixation with modern plates has recently been reported (Guerrero et al. 2019).

Due to these obvious problems of plate fixation Kappos and co-workers tested an adhesion barrier in plate fixated fractures of the proximal phalanx (Kappos et al. 2015). A methyl cellulose device was used to cover the dorsally placed plates with the intent to inhibit contact between the extensor tendon and the plate. However, follow-up could not show any long-term benefits of the adhesion barrier (Kappos et al. 2015).



*Figure 5. Plate fixation of proximal phalanx.*

## **External fixation**

External fixation is a very old invention described already in ancient Greece. It can be used provisionally or as sole treatment if applied correctly (Bible and Mir 2015). In finger fractures it is a technique most frequently used in difficult joint injuries, like PIP joint fracture dislocations, or in crush injuries with infection, tissue loss and comminuted fractures (Ashmead et al. 1992).

There are commercially available devices to use, but making your own system, dynamic or static, with K-wires, rubber bands, locking balls or bone cement is an option (Sraj 2016; Walter and Papandrea 2011; Zhang et al. 2017) (Figure 6).

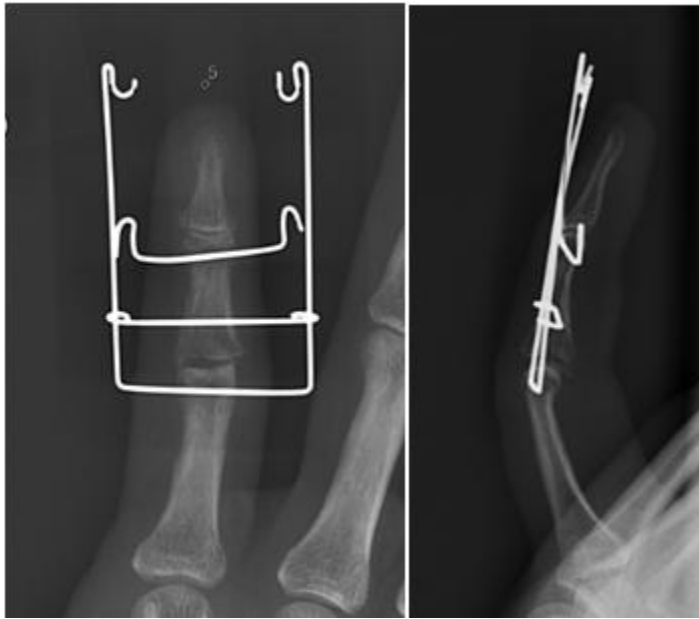


Figure 6. Dynamic external fixation for intra-articular PIP joint fracture.

## SURGICAL GLUES AND TISSUE ADHESIVES

Despite the various methods for osteosynthesis described above, there are situations with multifragmented fractures wherein a surgical glue with the ability to stick to bone and provide stability would be an appreciated contribution to treatment options. Surgical glue is not a novel invention in any way; rather the problem is that no product that has reached the market has been strong enough to use on fractured bone. For a glue to be useful in fracture surgery it needs to have a good adhesion ability to bone *in vivo*, hence in a wet environment, it must be strong when it cures in order to add to stability, it needs to be easy to use, it cannot be expensive, it has to be safe and must not affect the bone healing process in a negative way. Both the glue itself as well as its degradation products must be safe to use in the human body (Farrar 2012; Sierra and Salz 1996). Since fibrin was discovered as a sealant in the 1940s and cyanoacrylate was presented as potential surgical glue in the 1950s the research on tissue adhesives and surgical glues has been intense. Still, except for bone cement, no adhesive for use on bone has arrived for clinical use. This is mainly due two factors: Adhesion to bone has been poor and/or tissue toxicity has been too high (Farrar 2012).

Commercially available tissue adhesives and sealants in short:

- Fibrin sealant is a hemostat, an adhesive and a sealant. It can be used as an adhesive in peripheral nerve surgery, skin grafting, colon sealing and for hemostasis. It is a two-component product made from human or bovine fibrinogen and thrombin (Spotnitz 2010).
- Cyanoacrylate (N-butyl-2-cyanoacrylate) can be used for wound closure, for fixation of hernia mesh and off-label for hemostasis of gastric varices. The adhesion to bone tends to wear off with time. Its biggest disadvantage is its toxicity which makes it unsuitable for bone repair (Bhat et al. 2013; Ekelund and Nilsson 1991).
- GRF-glue (Gelatin Resorcinol Formol) is a sealant used primarily in aortic dissection and for hemostasis. The toxicity of the formaldehyde activator requires careful dosage (Scognamiglio et al. 2016).

- Albumin-based glues. Elastic seals are formed when albumin-glutaraldehyde bonds covalently to tissue surfaces. The albumin-based glues are stable and can be detected in repair sites for up to two years after a vascular anastomosis where it is used as a hemostat (Scognamiglio et al. 2016).
- Polysaccharide-based adhesives from dextran or chitosan are sealants suitable for sealing fistulas of the gut or for nerve repair (Scognamiglio et al. 2016; Serrano et al. 2017).
- Bone cement consists of poly(methyl methacrylate) (PMMA) and is the material used to secure joint replacements to bone. It actually works more as a filler than an adhesive. The cement only attaches mechanically to the porous bone, not the smooth cortex (Farrar 2012; Vaishya et al. 2013).
- Composite materials for dental purposes. These materials are related to bone cement and have developed rapidly during the decades following discovery of the so-called acid-etching technique in which an acrylate resin bonds to acid-etched enamel or dentin and rapidly cures upon exposure to light (Ikemura and Endo 2010).

Many other tissue adhesives and sealants are under development but are not yet available for commercial use. Mussel inspired adhesive is probably the most well-known. The mechanism for adhesion is the same as that used by mussels to adhere to rocks in the ocean, and DOPA is one of the substances that is being exploited in combination with hydrogels for the purpose of getting improved adhesion in wet environments (Barrett et al. 2013; Kim et al. 2014).

## **ADHESIONS AND ADHESION BARRIERS**

Stiffness of the finger joints caused by adhesions after surgery or immobilization is a common problem in hand surgery. It is often seen after tendon injuries, especially on the flexor side, and after fractures. The complicated healing process within the flexor tendon sheath has for many years been the focus of research around adhesion formation in hand surgery (Loiselle et al. 2016). The sliding system of the hand is complex and involves more structures than the flexor tendons and their sheath. This system has been explored by Guimberteau et al. and is described as the microvacuolar system. This system is delicate and complex and is affected by multiple types of trauma and surgical procedures. The complexity of the system and the fact that it is present all the way from the skin to tendons and bone, plays a part in explaining why adhesion barriers tested during the years only have had moderate effect (Guimberteau et al. 2010).

Adhesion barriers, both mechanical and/or substances that could reduce adhesion formation, have been tested in flexor tendon surgery since hand surgery itself was first defined. The first reference on this topic is from 1939 when cellophane was used as a permanent tendon sheath (Wheeldon 1939). Other materials and substances tested throughout the years include amnioplastin (Pinkerton 1942), vein grafts as tendon sheath (Strauch et al. 1985), polytetrafluoroethylene membranes or fascia (Hanff and Hagberg 1998; Peterson et al. 1990), sodium hyaluronate (Hagberg and Gerdin 1992), peritoneum parietale (Oei et al. 1996), fibrin sealant (Frykman et al. 1993; Jones et al. 2002), amniotic membrane (Demirkan et al. 2002), ADCON/T (Golash et al. 2003), bovine pericardium (Sungur et al. 2006), alginate (Namba et al. 2007), lactoferrin derived peptide (Hakansson et al. 2012; Wiig et al. 2014; Wiig et al. 2011), mannose-6-phosphate (Lees et al. 2015) and many more. Despite the research activity in this area there is at present, no product in wide clinical use.

Adhesion barriers in fracture surgery have not been as frequently reported on as for flexor tendon surgery. Covering a dorsally placed plate with an adiposal flap is an option that has been described in a case report with resulting good functional outcome (Lucchina et al. 2015). There is, as previously mentioned, an RCT by Kappos and coworkers, wherein a methyl cellulose membrane was used to cover dorsal plates on proximal phalangeal fractures. The small effect seen in preliminary results after six weeks did not persist in the six months follow-up. The results of this study have been debated, and the main point made by critics has been that there is a possibly incorrect assumption on the part of the authors that the adhesions after phalangeal fracture surgery are located on the dorsal side of the finger, in tissues surrounding the extensor tendon. According to the critics, the adhesions might just as well be located on the flexor side due to insufficient mobilization and could well explain the results of the study (Lees 2016).

In gynecology and spinal surgery, a gel called Oxiplex<sup>®</sup> has been used to prevent pain and adhesion formation after surgery. The gel consists of carboxy methyl cellulose (CMC) and poly ethylene oxide (PEG) and has been reported to reduce pain postoperatively (Assietti et al. 2008; Fuchs et al. 2014; Lei et al. 2013). This gel also exists in a formulation designed for hand surgery called Dynavisc<sup>®</sup>. Preliminary results for this product in tenolysis have been reported at the annual European hand surgery congress (FESSH) (Battiston B 2013; Di Guiseppe P 2015) and in an unpublished rabbit study (Riccio). In nerve surgery on the hand, there is a study on revision surgery in carpal tunnel syndrome combined with Canaletto device (an implant sutured to the ends of the cut flexor retinaculum that widens the gliding canal for nerve and tendons) which has showed modest positive results (Carmona et al. 2018). No reports on Dynavisc<sup>®</sup> in fracture surgery have yet been published. According to the manufacturer, Dynavisc<sup>®</sup> is a mechanical adhesion barrier that reduces postoperative inflammation which in turn reduces postoperative pain.

## REHABILITATION

Rehabilitation after treatment of finger fractures is essential for the outcome, regardless of type of osteosynthesis or immobilization. In conservative treatment the nature of the fracture determines the aggressiveness of the rehabilitation as previously described. To serially modify splints is one way to gradually allow a larger arc of motion over time (Feehan 2003).

In the case of rehabilitation after open reduction and internal fixation, early postoperative mobilization should start sometime during the first postoperative week (Ataker et al. 2017; LaStayo et al. 2003). Until then, edema control and immobilization are the best treatments to protect the hand during the inflammatory phase just after surgery (Freeland et al. 2003). An early start is important since most of the recovery in terms of pain, strength, range of motion and hand use occurs by week 6 postoperatively (Miller et al. 2017). A protective splint in between rehabilitation sessions is recommended (Freeland et al. 2003). There are many different regimes for early active mobilization, for example Miller and coworkers compared two regimes of active mobilization in an RCT in order to establish whether they could improve outcome regarding PIP joint extension lag. One group performed their exercises with constrained MCP joints and the other group with unconstrained MCP joints. However, no difference was found between the groups regarding PIP joint extension lag, TAM, strength or pain (Miller et al. 2016).

## AIMS

The overall aim of this thesis was to investigate different methods to improve outcome for patients with middle and proximal phalangeal fractures. Based on the identified postoperative complications, new methods for preventing adhesions and for fracture fixation were explored.

The specific aims were:

1. To retrospectively describe reoperation rate and postoperative complications based on fracture type and operation methods in patients operated for closed extra-articular middle and proximal phalanx fractures in our department, and to describe demographics in this patient group.
2. To evaluate a new material, a thiol-ene composite, for bone repair both *in vitro*, in a biomechanical fatigue test, and *in vivo* regarding safety, bone healing, inflammation and adhesive properties to bone.
3. To explore the effect of Dynavisc<sup>®</sup>, an adhesion barrier designed for hand surgery, in ORIF with plate and screws in proximal phalanx osteosynthesis.
4. To evaluate a thiol-ene composite coating used on metal plates as an adhesion barrier in a rabbit model.

# MATERIALS, PATIENTS AND METHODS

## Study populations (Paper I and III)

In Paper I and III the study populations were treated at the Department of Hand surgery at Södersjukhuset, Stockholm, Sweden.

In Paper I HAKIR, the Swedish quality registry for hand surgery, was used to identify all patients operated for a phalangeal fracture at the Department of Hand surgery at Södersjukhuset from February 2010 to December 2014 (HAKIR 2014). Patient charts and radiographs were examined after excluding children, open injuries, thumb fractures, fractures of the distal phalanx and intra-articular fractures. Starting with 775 registered phalangeal fractures a total of 181 fractures in 159 patients were included in the study. The charts and radiographs were thoroughly checked by two investigators (JvK and JN) with regard to fracture type, operation method, reoperations, sick-leave, injury mechanism, age and gender.

In Paper III, ten patients between 18 and 70 years of age requiring ORIF of proximal phalanx due to a fracture or a malunion, but with a normal range of motion, were included after informed consent from March 2016 to September 2017. Exclusion criteria were open injuries, intra-articular injuries, associated injuries distal to the wrist, joint disease and inability to follow a postoperative rehabilitation program. The initial plan for this study was to conduct an RCT on Dynavisc® in plate osteosynthesis of the proximal phalanx. The primary outcome was TAM at three months and the significant level was set to less than 20° difference from the contralateral healthy finger. Power calculations indicated a need for 64 patients in each group to reach statistically significant results, but to allow for drop-outs planning was made for 80 patients per group. Since such a large study would be both time-consuming and expensive, a pilot study was conducted first.

## Fiber reinforced adhesive patch (FRAP) (Paper II)

The second paper reports on a new material for bone repair, a thiol-ene composite, in a fiber reinforced adhesive patch (FRAP)(Nordberg et al. 2007). The patches are built up from the bone surface in layers, starting with preparation of the bone surface. The first step after reduction of the fracture is to remove the periosteum on both sides of the fracture and wipe the bone surface dry. A primer is then applied on the bone and dried by air flow (Hed Y 2013; Nordberg et al. 2010). The second step is application of the matrix material and the third is a fiber layer consisting of a surgical mesh. The construction is cured by irradiation of the surface with high energy visible light (HEV) using a LED-lamp Bluephase® 20i which activates the photo-initiator in the primer and matrix, thereby initiating the polymerization. Steps two and three are repeated until the construction is sufficiently rigid (in this case three layers of fibers). The final measure is to cover the FRAP with one last matrix layer yielding a smooth surface (Figure 7).



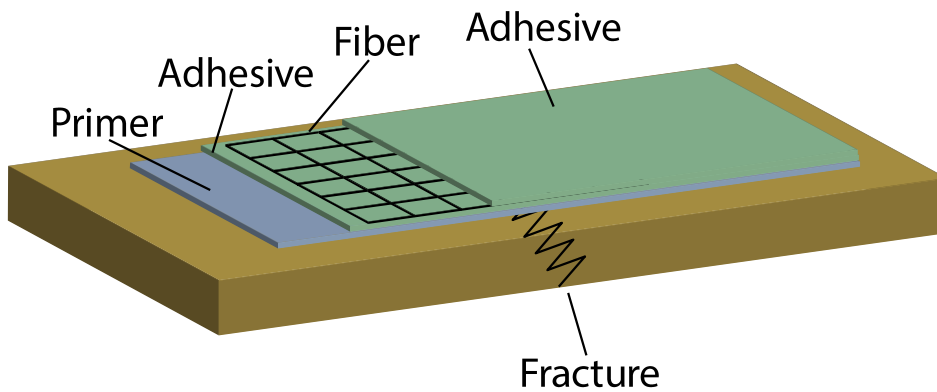


Figure 7. Schematic build-up of FRAP.

Primer: BAPA derivatives with ETTMP as crosslinker

Adhesive: TEMPIC TATATO with a hydroxy apatite filler (56 wt%)

Fiber: Hernia mesh (PET).

### Three-point bending test (Paper II)

The FRAP-concept was tested mechanically in Paper II. The *in vitro* test on transverse and oblique fractures on porcine metacarpal bones was carried out using a three-point bending test (Instron 5566, Instron Korea LLC) (Figure 8). The fractures were reduced and fixed with FRAP, crossed 1 mm K-wires or AO compact hand 1.5 plates (Figure 9). In the first series samples were forced until breaking point was reached (previously unpublished). In the second, a fatigue test was performed in a dynamic set-up. Forces between 10-70 N were applied periodically for 1000 cycles with the purpose of simulating hand rehabilitation exercises with a good margin of the force needed (Edsfeldt et al. 2015; Yang et al. 2016). The movement in the fracture was compared between the different fixation techniques.

The operated rat femurs included in Paper II were also evaluated using the three-point bending technique after the *in vivo* study on rat. The purpose was to compare the strength of the healed bone in FRAP-treated femurs to the ones treated with a more conventional technique with a RatFix<sup>®</sup> plate and to compare to native non-operated bone.

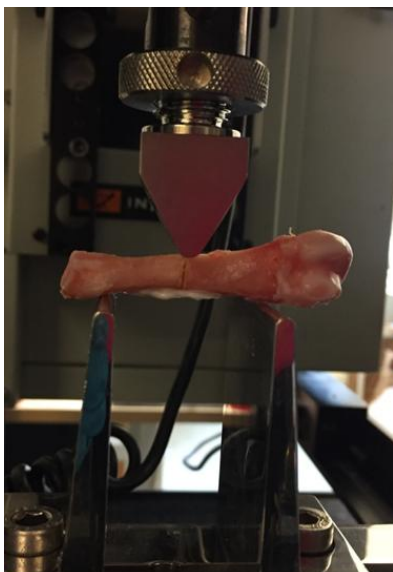
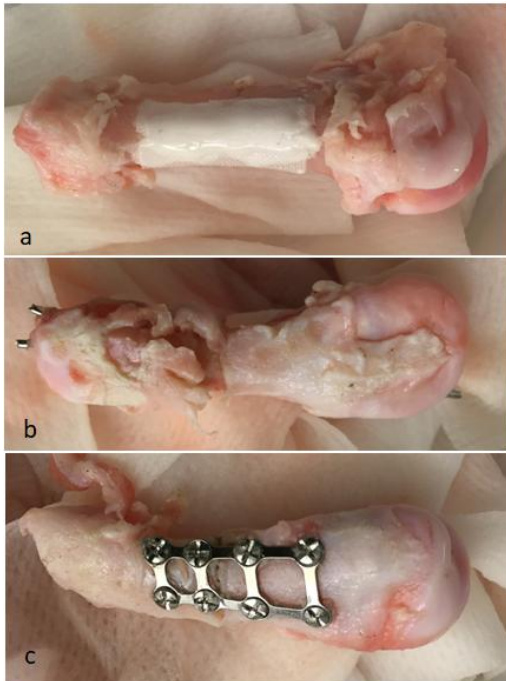


Figure 8. Instron 3-point bending set-up.



*Figure 9. Osteosynthesis for porcine metacarpal mechanical testing. a) FRAP, b) crossed K-wires c) AO compact hand 1.5 on transverse fracture of porcine metacarpal bone.*

### ***In vivo* study of FRAP on rat femur (Paper II)**

A rat femur fracture model was used to evaluate biocompatibility of the FRAP *in vivo* in Paper II.

Four groups of rats were studied:

1. Fracture of the femur fixed with a RatFix<sup>®</sup> plate and a FRAP (n=13)
2. Fracture of the femur fixed with a RatFix<sup>®</sup> only (n=9)
3. No fracture but a FRAP applied for study of the adhesion strength and for studies of inflammation (n=12)
4. No fracture but a FRAP for inflammation studies (n=4)

The surgeries were performed under general anaesthesia on female Sprague Dawley rats. The fur over the hind leg was shaved and the skin sterilized. A straight incision was made over the lateral border of the femur just distal to the hip ending proximal to the knee. The fascia lata was opened and the femur exposed by blunt dissection of the m. vastus lateralis and m. biceps femoris. The dissection was circumferent at the site of osteotomy.

Rat femurs were fractured using a thin,  $\varnothing$  0.2 mm gigly saw. The fracture was reduced and stabilized using RatFix<sup>®</sup>, a plate with screws designed for rat femur, by RIsystem AG, Switzerland. In the first group, a FRAP with three fiber layers was built up over the fracture in addition to the RatFix<sup>®</sup>. In the third group a FRAP was built up on unfractured bone with a “tail” of fiber sticking out on one end to be used as a handle for a peel test (Figure 10).

The muscle and the fascia were sutured back with Vicryl 4/0 in two layers. The skin was closed with an intracutaneous running suture of Monocryl 5/0. Postoperative X-ray was carried out in all cases (Figure 11). All surgeries were performed by the same surgeon (JvK). Rats were housed 3-4 in each cage and were allowed free

mobilization of the operated leg. They had access to food and water and were assessed regarding pain and wound status on a daily basis. Pain was managed with caprofen postoperatively and was administered for two days after surgery.

After five weeks all the rats were euthanized, and the healing of their femurs was assessed with X-ray. The hind leg was dissected by exarticulation of the hip and the knee. Soft tissues were carefully dissected under ocular inspection and documentation. The femurs were examined by microcomputed tomography to evaluate the healing process, histology to assess inflammation and bone healing, three-point bending test for mechanical strength, and visual inspection to examine adhesions and other effects on surrounding soft tissue. Adhesion strength of the FRAP in the unfractured femurs was evaluated by a peel test.

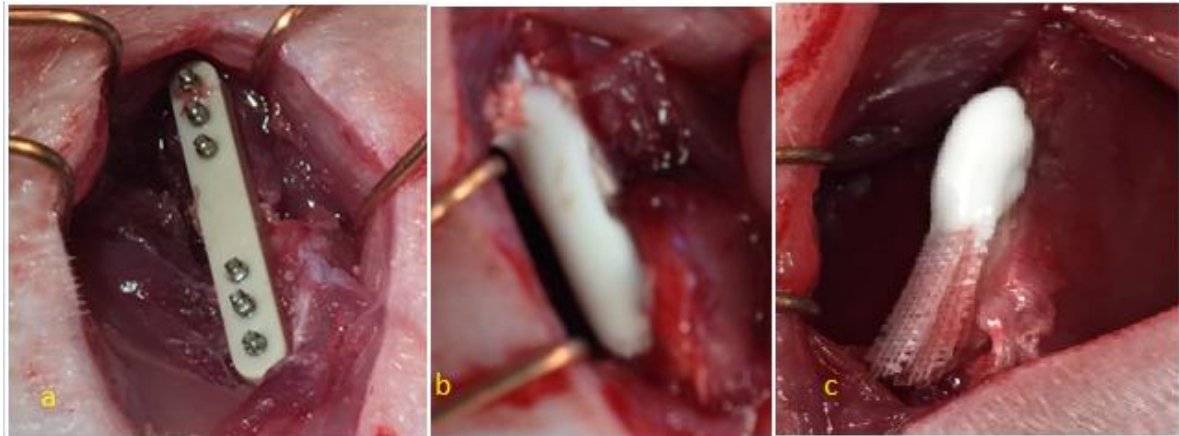


Figure 10. Intraoperative: a) RatFix<sup>®</sup>, b) FRAP, c) FRAP designed for peel test.

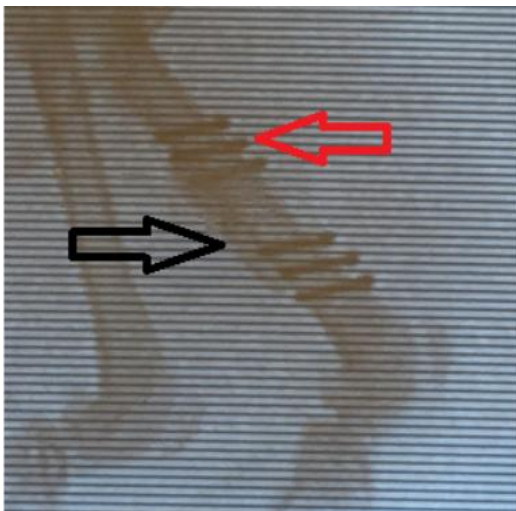


Figure 11. Radiograph of femur with RatFix<sup>®</sup> (red arrow) and FRAP (black arrow).

### Peel test (Paper II)

The peel test was performed after five weeks *in vivo* and data was compared to a newly made FRAP on the contralateral femur just after the rats were euthanized. After dissection of the rat femurs they were attached to a Planar Biaxial TestBench Instrument (TA Instruments–ElectroForce System Group, Eden Prairie, MN, USA) and peel test was conducted. Force was measured and the maximum load and the width of the FRAP were used to calculate peel strength.

## **Other tests performed on FRAP (Paper II)**

Short and general descriptions. More detailed descriptions are available in Paper II.

### *Microcomputed tomography ( $\mu$ -CT)*

All 9 femurs with RatFix<sup>®</sup> only, all 13 femurs with RatFix<sup>®</sup> and FRAP and three unoperated intact femurs were examined.

$\mu$ CT (SkyScan 1176, Bruker microCT, Kontich, Belgium), was used. Mineral density (BMD), in  $\text{g m}^{-3}$  of the newly formed bone, total bone volume (BV) in  $\text{m}^3$ , bone volume fraction of tissue volume (BV/TV), and mean cross sectional bone area in  $\text{m}^2$  were analyzed. Intact bone was used for comparison. All the examinations were performed via Research Institutes of Sweden (RISE).

### *Histology*

Inflammatory reactions and bone healing properties were studied in three femurs each from the groups fixed by RatFix<sup>®</sup> only, RatFix<sup>®</sup> and FRAP and unfractured bones with a FRAP attached. The bones were fixated in 4% PFA, embedded in resin, and sectioned and stained with toluidine blue. All samples were handled by Histolab and the results were analyzed via RISE.

### *Biocompatibility studies*

Biocompatibility studies on FRAP material in Paper II were performed by RISE and NAMSA, a contract research organization for medical devices, and regarded evaluation cytotoxicity, genotoxicity and irritation. All studies were performed under Good Laboratory Practice (GLP).

## **Operative treatment and rehabilitation (Paper III)**

Ten consecutive patients were operated for a proximal phalangeal fracture or a corrective osteotomy of the proximal phalanx fixed with plates and screws. A dorsal tendon splitting exploration technique was used. After osteosynthesis, the plate was covered with Dynavisc<sup>®</sup>, a gel designed to prevent adhesions in hand surgery. The tendon was repaired and subsequently Dynavisc<sup>®</sup> was applied between the extensor tendon and the skin before skin closure. The total amount of Dynavisc<sup>®</sup> used was 1 ml which is the volume of one dose and the appropriate amount for use in one finger. All patients included in the study gave their written consent to participation.

Patients were immobilized in a cast until start of rehabilitation which was initiated 1-4 days postoperatively. Rehabilitation consisted of full active motion exercises with at least 5 repetitions every other hour using a static splint between exercises if needed. All rehabilitation and follow-up were conducted by the same, experienced physiotherapist (JR). Primary outcome was TAM at three months; secondary outcomes were pain at rest, pain on motion and grip strength. Measurements were performed at start of rehabilitation, after two weeks, after three months and finally after one year. TAM was evaluated by goniometry, pain was assessed using a visual analogue scale (VAS) and grip strength was measured with a Jamar dynamometer (Jensen et al. 1986; Mathiowetz et al. 1984). Early endpoint at three months was chosen to reveal a potential true effect of Dynavisc<sup>®</sup> which, according to the manufacturer, is resorbed within 30 days after administration.



### ***In vivo* study of DendroPrime in a rabbit model (Paper IV)**

Following on from the matrix of the FRAP described in Paper II, the thiol-ene composite went through further chemical development, resulting in an even better attachment to the underlying surface. The concept of coating a metal plate with the material to prevent adhesion formation between the plate and surrounding soft tissue was named DendroPrime.

Twelve rabbits were operated on the second toe of both hind paws under general anaesthesia. The surgeries were performed in a sterile environment after shaving of the paws by two surgeons (JvK and HA). A straight incision was made on the plantar side of the base of the second toe. The flexor tendon sheath was opened, and the periosteum and cortex of the phalangeal bone was scratched simulating an injury to the bone. An AO compact hand 1.3 straight plate was then attached with two screws. A complete fracture was not an option due to the small dimension of the bone. On one of the toes of each rabbit the plate was coated with DendroPrime through an initial addition of the primer to the metal plate, followed by subsequent coating of plate with the thiol-ene composite and curing by using HEV-light (Figure 12). On the contra-lateral toe the plate was left bare, and on both toes the flexor tendon sheath was closed with 5/0 PDS sutures, allowing the flexor tendons to glide freely over the DendroPrime and the plate. The skin was closed with an intracutaneous running suture with Monocryl 5/0. Four rabbits were kept unoperated for comparison.

The rabbits were checked on daily and pain was managed by injections of buprenorfin for five days postoperatively. The rabbits had free access to pellets, water and fresh fruits and vegetables. After seven weeks of free mobilization the 16 rabbits were euthanized. The operated toes were carefully dissected and examined by ocular inspection for adhesions. Biomechanical testing was carried out using a model developed by Olmarker et al. The toe was attached to a tension testing device Planar Biaxial TestBench Instrument (TA Instruments - ElectroForce System Group, Eden Prairie, MN, USA, and the FDP-tendon was pulled with increasing forces (Olmarker et al. 2010). The process was filmed and at specific forces a frame taken from the film was analysed using Image J software (version 1.52i). From these photos the angles of the toe joints were measured multiple times by two separate investigators (JvK and HA).



**Figure 12.** a) *Intra operative plate* and b) *DendroPrime coated plate* c) *Postoperative X-ray of the rabbit toes.*

## **Statistics**

In all Papers SPSS software version 17 was used for statistical calculations and a p-value of  $<0.05$  was considered statistically significant. (CI 95%)

In Paper I, a logistic regression analysis was performed to assess whether operation method was the only factor associated with reoperation or if fracture type had influence on the reoperation rate.

In Paper II, a two-sided Mann-Whitney U-test was used in the peel-test of adhesion strength.

In Paper IV, Wilcoxon rank sign test was used for comparison between toes with coated and uncoated plates. For comparison between non-operated toes and bare plates the one-way ANOVA with Tukey HSD posthoc was used.

## **Ethics**

All studies in this thesis were approved by the regional ethics committees, and the studies with human subjects were performed in accordance with the Helsinki declaration (2013).

# RESULTS

## Paper I

In this study reoperation was primary outcome variable, and 47 fractures in 36 patients were reoperated for the reasons shown in Table 1. The majority of reoperated fractures were stabilized with a plate, although a plate was the least used method for primary fracture fixation (Table 1). The most frequent reasons for reoperations, responsible for 68% of all reoperations, was adhesions and joint stiffness (Table 1). Another finding was that plates were more commonly used in comminuted fractures (Table 2). The logistic regression analysis showed an increased risk of reoperation after plate fixation with a statistically significant OR of 2.249 ( $p=0.047$ ). After adjusting for fracture type the value was not significant, OR 2.194 ( $p=0.091$ ) (CI 95%).

Table 1. Reason for reoperations.

	K-wires	Screws	Plate	Total
Local problems of osteosynthesis material	8	4	1	13
Adhesions/joint stiffness	7	5	20	32
Redislocation of the fracture	0	1	0	1
Rotational malunion	0	0	1	1
Total	15	10	22	47

Table 2. Osteosynthesis method for different fracture types

Fracture type	Osteosynthesis method			
	K-wires	Screws	Plate	Total
Comminuted	8	8	29	45
Spiral/Oblique	6	57	7	70
Transverse	47	2	16	65
Total	61	67	52	181

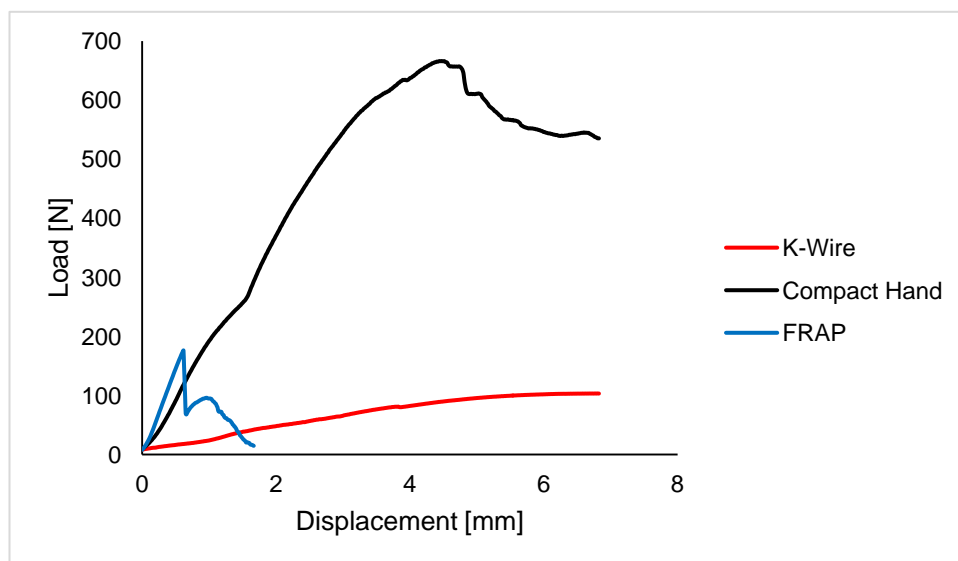
Demographic results from this study revealed a rather even sex distribution in these fractures, 77 women and 82 men. Mean and median age was 43 (14-88) years. Fall injuries were by far the most common mechanism of injury followed by twisting forces and sports injuries. The proximal phalanx was affected more often than the middle phalanx, 88% vs.12%. The ring- and/or the little fingers were affected in 77% of all cases.

The median sick-leave time was 49 (0-300) days. Reoperated patients had a longer sick-leave; 85 (0-300) days compared to 39(0-207) days for those not reoperated.

## Paper II

### *Biomechanical testing*

Figure 13 shows the previously unpublished results from a series of load of porcine metacarpal transverse fractures until breaking point in the three-point bending test. The FRAP resisted forces up to 176 N before it broke or detached from bone. Figure 15 shows the displacement of the fracture for different osteosynthesis methods. K-wires were bent, obviously, they never broke or detached.



*Figure 13. Loads until breaking point for fixated transverse fractures of porcine metacarpals in a three-point bending test.*

Figure 14 shows results from the dynamic fatigue test in which forces between 10-70 N were applied to porcine metacarpal, transverse fractures stabilized with AO Compact hand plate 1.5, K-wires or FRAP respectively in a three-point bending test. Figure 14a shows the displacement to cycle curve in the different techniques and Figure 14b shows the displacement curve of first load. Results indicate that FRAP is



as stable and rigid as a plate up to a certain load, being lower than metal plates but higher than K-wires.

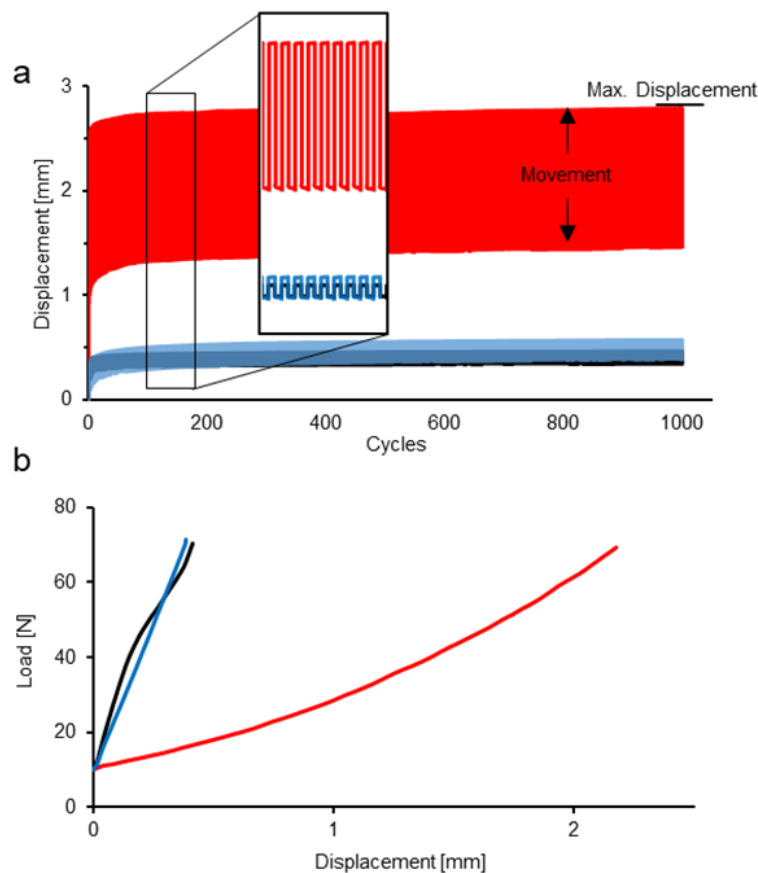


Figure 14. a) Displacement of fracture in fatigue test of porcine metacarpal transverse fractures fixated with K-wires (red), AO Compact hand 1.5 plate (black) and FRAP (blue). b) Displacement curve of first load in cyclic three-point bending test in porcine metacarpal transverse fractures fixated with K-wires (red), AO Compact hand 1.5 plate (black) and FRAP (blue).

#### *In vivo study of rat femur*

Two rats bit on their sutures during the first postoperative night, resulting in wound ruptures. Both rats were anesthetized the next morning, and the wounds were resutured. Wound healing proceeded without complications thereafter.

Radiographs at endpoint 5 weeks postop showed normal bone healing in all fractured femurs with RatFix<sup>®</sup> or RatFix<sup>®</sup>+FRAP. Ocular inspection at dissection showed no negative effect on bone healing and no signs of inflammation or adhesion formation around the FRAPs. It was noted that muscle tissue did not adhere at all to the FRAP material which was an evidently different from the RatFix<sup>®</sup> where adhesions were massive (Figure 15) (Previously unpublished results).

#### *Histology*

Histology showed no signs of inflammation in the area between FRAP and soft tissue, and there was no negative effect on bone healing in the presence of FRAP (Figure 16).

### *Peel test*

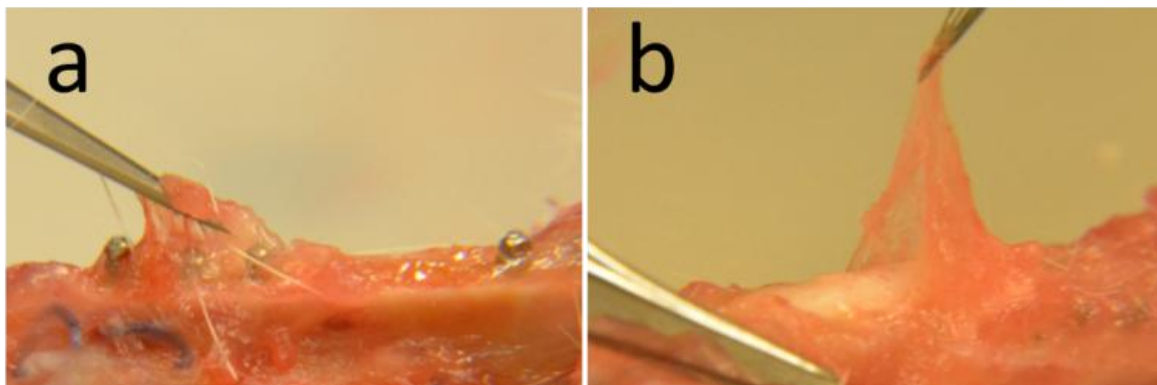
Peel test results showed that FRAP maintained 60% of its bond strength to bone after five weeks *in vivo*.

### *$\mu$ -CT*

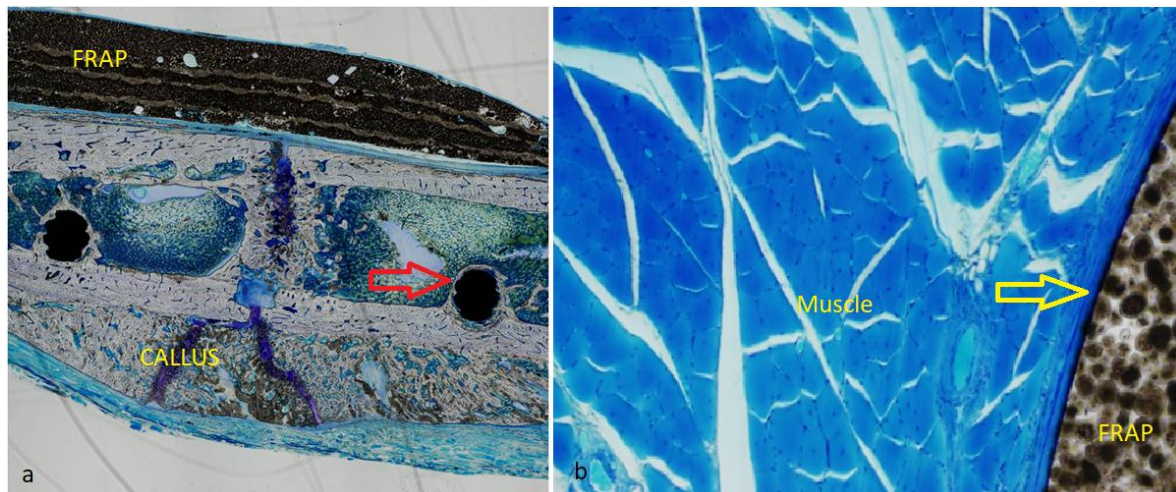
Results from  $\mu$ -CT and three-point bending test showed no significant differences between the group fixed with RatFix<sup>®</sup> and RatFix<sup>®</sup>+FRAP.

### *Biocompatibility studies*

Safety evaluation under GLP according to ISO 10993 showed that FRAP leachables are safe regarding cytotoxicity and genotoxicity



*Figure 15. Dissection of rat femur after five weeks in vivo: a) Massive adhesion formation between RatFix<sup>®</sup> and surrounding soft tissue. b) No adhesions between FRAP and surrounding soft tissue.*



*Figure 16. a) Healed fracture with a hole after a RatFix<sup>®</sup> screw (red arrow) but FRAP still in place with fiber layers clearly visible. b) No signs of inflammation between FRAP and muscle (yellow arrow).*

### Paper III

Seven men and three women were included. Mean age was 44 (31-61) years. Eight cases were acute fractures, two were correction osteotomies after a previous fracture resulting in rotational malunion but normal joint mobility.

In all patients TAM was classified according to Page and Stern (Page and Stern 1998) where an 'Excellent' results means a TAM>240°, 'Good' means TAM 220°-239°, 'Fair' is TAM 180°-219° and 'Poor' is TAM <179°.

At the primary endpoint, TAM at three months, only two patients had reached the significant level of a TAM with less than 20° difference compared to the contralateral finger. After one year five patients had reached this level. The median difference in the group was 45° at three months and 23.5° at one year. Regarding pain five patients complained of pain on motion at three months. The patients with persisting pain with VAS on motion of 8 or more after one year were also the ones with the worst outcome regarding TAM, scoring only 'Fair' in the Page and Stern classification of outcome (Table 3).

*Table 3. Results on TAM and pain. (TAM classification according to Page and Stern.)*

	Three months			One year		
Patient	TAM classification	Pain at rest	Pain on motion	TAM classification	Pain at rest	Pain on motion
1	Good	5	50	Good	0	0
2	Good	0	0	Good	0	0
3	Excellent	0	0	Excellent	0	0
4	Fair	0	0	Excellent	0	0
5	Poor	0	73	Fair	0	45
6	Poor	4	20	Fair	2	8
7	Excellent	0	18	Excellent	0	0
8	Poor	0	0	Fair	0	23
9	Poor	0	39	Fair	0	15
10	Excellent	0	0	Excellent	0	4

## Paper IV

One rabbit bit on the wound and opened up the skin suture of one paw on the third postoperative day. The tendon sheath was still intact. This was noted on the daily check-up and the wound was resutured without complications.

The biomechanical results of the *in vivo* study on rabbits showed that surgery of the toe had reduced DIP joint mobility. A bare plate under the tendon reduced the mobility more than if the plate was coated with DendroPrime (Figure 17). These results were statistically significant in forces of 1, 3, 4 and 5 N (but not in 0.5 N  $p=0.06$  or 2 N  $p=0.08$ )

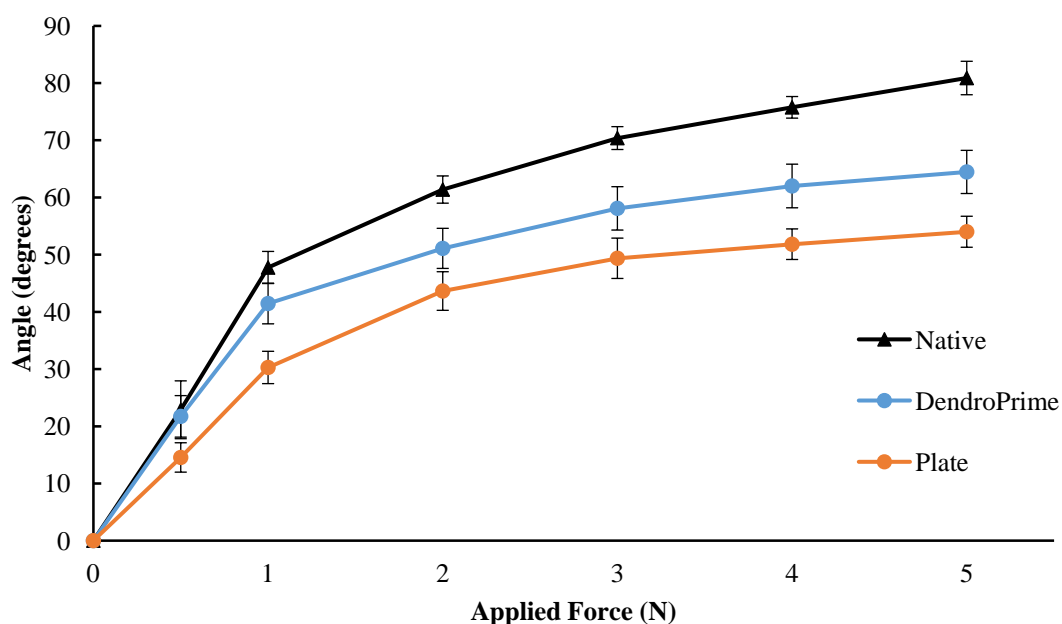


Figure 17. The measurements of DIP joint angle at the pulling forces of 0.5, 1, 2, 3, 4 and 5 N. The points are mean values and the error bars show SEM.

Ocular inspection of the dissected toes suggests that DendroPrime inhibits soft tissue adhesion (Figure 18). The flexor tendons did not adhere as much to the Dendroprime coated plates as the metal in the bare plates.

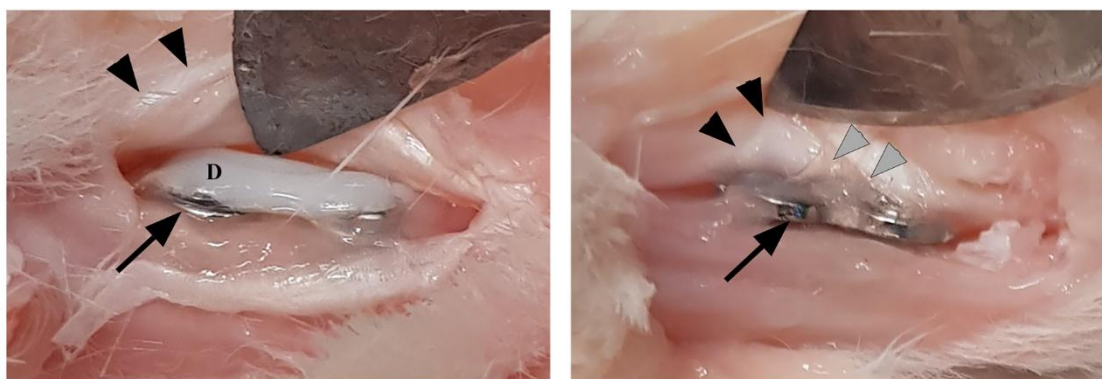


Figure 18. DendroPrime (D) (left) shows no adhesions to the tendons (black arrows), bare plate (right) reveals adhesion formation (grey arrows) between plate and tendons.

## DISCUSSION

This project started from an ambition to follow up on the results in our own department after finger fracture surgery. We had a suspicion there was quite a large number of reoperations for unplanned hardware removal and tenolysis after phalanx fracture surgery in our department, and a desire to investigate the root causes became the main reason for conducting the first study in this PhD project. It turned out the suspicion was well merited.

The primary finding in Paper I was a 42% reoperation rate in plate fixated phalangeal fractures indicating a substantial problem with plate fixations. The reoperations were not due to fracture redislocations but to finger stiffness. High reoperation rates have previously been reported by others (Kurzen et al. 2006; Page and Stern 1998; Pun et al. 1991). The last decades have brought new, thinner plates to the market, but this does not seem to have had an effect on outcome. In fact, Guerrero et al. and Brei-Thoma et al. showed very similar reoperation rate as in our study, 39% and 44% respectively (Brei-Thoma et al. 2015; Guerrero et al. 2019). Modern thin plates were designed to be left in place, but still very often have to be removed. Should plate fixation of phalanges be considered as a two-stage procedure or could these problems be prevented by other materials or techniques?

Extraction of osteosynthesis material is a costly procedure in orthopaedic surgery (Bostman and Pihlajamäki 1996). In a study by Reith et al. 72% of patients gained a better functional outcome after plate removal, but 10% had complications after the procedure (Reith et al. 2015).

Finger stiffness was the dominating complication after finger fracture surgery in our study, and there was only one reoperation due to redislocation of the fracture. Could we have reached better results with fewer reoperations using a more aggressive rehabilitation program postoperatively? This topic was beyond the scope of this thesis work but should perhaps be studied further.

The gender distribution for finger fractures was very even in our study, which differs from the literature reporting that men usually are more commonly affected than women (De Jonge et al. 1994). A possible difference can be that we only included closed injuries. Open fractures caused by different tools and machines might be more common in male-dominated occupations (De Jonge et al. 1994).

The most obvious limitation of Paper I is the retrospective design that relies on patients' charts and with little data on finger mobility and functional outcome. Also, including middle phalanx fractures might have made the analysis of results more complex, since middle phalanx fractures are different in their nature compared to proximal phalanx fractures. However, middle phalanx fractures were few in numbers and should not have severe impact on the results.

The foremost strength of our study is the large number of fractures included and the consecutive series of all patients operated during the study period. Another benefit of the study is that neither metacarpal fractures nor open or intra-articular fractures were included, making the patient material more homogenous than in other studies.

The scientific projects using polymer chemistry started by chance when we heard about a new concept for fracture fixation being developed by a group of scientists at the Royal Institute of Technology (KTH). We made contact and collaboration started which ultimately resulted in Paper II and IV of this PhD project.

Paper II was the first translational study and it has been challenging in many ways. A multidisciplinary team of chemists, biologists, medical doctors and engineers, working together on the same project, preparing manuscripts and for journals out of their respective fields presents enormous opportunities for excitement but comes with unique challenges and, at times, frustrations.

In Paper II a completely novel concept for bone repair is presented. We have shown that the invented material actually adheres to living bone, does not disturb the fracture healing and it appears to be biocompatible. The incidental finding that the material in the top layer of the fixation material in the FRAP did not cause any adhesions to surrounding soft tissue was for a hand surgeon perhaps the most exciting discovery and generated the idea that led to Paper IV.

The animal model used in Paper II had some disadvantages. The load that rats put on their hind leg while playing and climbing in their cages is great and there is no way to provide external support to the leg during fracture healing. This was the reason for using an additional fixation to the FRAP in form of the RatFix<sup>®</sup>. The main purpose of the study was to evaluate effects bone healing, safety aspects of the FRAP, as well as bond strength to bone after fracture healing. We did not know *a priori* if the concept would be able to fixate the rat femur without any other support. We have not identified any small animal model where only minor load on the injured limb could be expected after fracture fixation. Even though we could not prove the value of the FRAP as a single concept for fracture fixation in Paper II, the results were still very promising regarding the properties of the material in itself and the anti-adhesive potential that was discovered.

The number of rats in Paper II was reduced to a minimum in according to the established ethical rules in research on animals. Hence the limited number of specimens included in the statistical calculations.

In the hand, a proximal phalangeal fracture typically angulates volarly (Barton 1984). If the fracture is stabilized with plate and screws, as described previously, the placement of that plate is dorsal or lateral. However, in the biomechanical studies in Paper II the three-point bending test simulated a fracture with a plate on the volar side loaded on the opposite side (Figure 8). This was necessary due to the testing device, and the anatomy of rat and pig bone, but did not quite represent pathophysiological conditions. The tests could be considered more relevant for other fracture types, like metacarpal fractures which angulates dorsally.

Another aspect of the biomechanical testing that could be discussed is the 'unfairness' of comparing the weak K-wires with a metal plate and a rigid FRAP. This makes the K-wires, a true workhorse in fracture surgery, look like a poor option. What must be kept in mind, is that K-wires have the fantastic advantage of being a method which can provide some stability after a *closed* reduction without ruining the microvacuolar system (Guimberteau et al. 2010). This obviously requires that safe entry points are respected (Rex et al. 2015). It is impossible to compare all aspects of different fracture fixation techniques only by biomechanical analyses of fractured bone without soft tissue.

Our investigations in Paper I made us realize that adhesion formation clearly is a significant problem in phalangeal fracture surgery. One way of preventing them is obviously active and early rehabilitation programs (Miller et al. 2017), but we asked the question: What if we could operate them differently, or add something to current treatment that would decrease the problem?



Right about this time a new CE-marked product, marketed in Europe, was presented to us; Dynavisc®. It was sold as an adhesion barrier appropriate for tenolysis and nerve surgery in the hand, and was claimed to decrease inflammation and work as a physical barrier. Poor scientific evidence for the anti-adhesive effect of the product in hand surgery was available in spite of it being sold throughout Europe. Having realized the problems of adhesions in finger fracture surgery, we were inspired to test this new product as an adhesion barrier in plate fixation of the proximal phalanx. One advantage of the study model we developed using an adhesion barrier in fracture surgery is that the base line range of motion in fractures finger could be expected to be normal, in contrast to studying the antiadhesive effects in tenolysis patients, for instance after previous flexor tendon repairs.

Paper III started with a plan to conduct an RCT with Dynavisc® compared to no additional treatment in plate fixation of proximal phalangeal fractures. Conducting a high-level study seemed important to justify costs of new products introduced on the market, and studies of this kind are rare in hand surgery (Schadel-Hopfner et al. 2008). Conducting an RCT however, is also very costly and may take considerable time. We therefore started with a pilot study of ten patients. The number of patients was decided mainly for practical and economic reasons and is of course, together with the lack of a control group the main drawback of Paper III. Since Dynavisc® has been claimed to have anti-inflammatory properties, using it on metal plates, placed just beneath the extensor tendon was very appealing. It is a known fact that metal plates, both of titanium and steel, cause inflammation that increases with time in the vicinity of tendons (Nazzal et al. 2006). If Dynavisc® could reduce that inflammation, would the joint mobility improve?

The results of the pilot study showed that only two patients had reached the decided significant level of total active motion within three months. Since Dynavisc® is resorbed after 30 days, effects of the gel alone later in the rehabilitation period seemed unlikely. Failure to identify positive effects of Dynavisc® in our pilot study made us refrain from starting the planned RCT.

One interesting finding in the Dynavisc® study was the further improvement of TAM that took place between three months and one year postoperatively. In contrast, previous research has reported that very little improvement occurs later than week six after surgery (Miller et al. 2017). Our results indicate that persistent and effective physiotherapy also after six weeks may be beneficial.

Another intriguing result is that the patients who reported the highest levels of pain on pain postoperatively were the ones who had the worst outcome regarding joint motion, both at three months and at one year. Postoperative pain control may be more important for end results than previously considered and identifying patients prone to high pain levels are probably very important in the rehabilitation process.

Based on the results of the *in vivo* study in Paper II, in which there was a total absence of adhesion formation between the FRAP surface the surrounding soft tissue, the idea of Paper IV developed. If the adhesive from FRAP could work as an adhesion barrier in plate fixation adjacent to tendons, joint mobility after fracture surgery might improve.

The results in Paper IV showed small, but statistically significant differences in DIP-joint mobility in favour of DendroPrime coated plates compared to bare plates. Based on the results from the ocular inspection that revealed more visible adhesions around the bare plates compared to the coated ones, one would have expected

larger differences in range of motion. We believe that one reason for the small difference could be that the FDS tendon decreased the contact area between the FDP and the underlying plate, with or without DendroPrime coating. Another reason could be the completely free and active mobilization that the rabbits were allowed, which decreased effect of the adhesions overall.

In respect of the animals, the number of rabbits was kept to a minimum This is an imposed but necessary drawback to the study.

DendroPrime showed no signs of degradation after seven weeks *in vivo* which indicates that it could serve for a considerable amount of time as an adhesion barrier and protect the tendon from the inflammation that increases over time in the presence of a metal plate (Nazzal et al. 2006). Hopefully this would mean a long-standing benefit from the use of this adhesion barrier compared to previous studies (Kappos et al. 2015).



## CONCLUSIONS

Reoperations after osteosynthesis of phalangeal fractures are common, especially in comminuted fractures fixated with a plate. Finger joint stiffness due to adhesion formation is the primary reason for reoperation.

FRAP, a new concept for bone repair based on TEC chemistry, shows high biocompatibility, and is safe to use regarding cytotoxicity, genotoxicity and inflammation. It does not inhibit bone healing and adheres well to bone even after five weeks *in vivo*. Biomechanical testing suggests it is strong enough for loads needed for rehabilitation after phalangeal fractures.

The use of Dynavisc® as an adhesion barrier in fracture surgery with plates does not appear to result in fewer postoperative problems.

DendroPrime, a coating for metal plates developed from the FRAP adhesive, displays adhesion barrier abilities. In a rabbit model, DendroPrime coating on plates resulted in better DIP joint mobility and less adhesions compared to bare plates.

## FUTURE PERSPECTIVES

Phalangeal fractures are common. Most of the fractures are treated conservatively in orthopaedic departments. Few of the patients require surgery, and only a small proportion of them are treated at a hand surgery department. These small numbers in combination with many different fracture patterns and associated injuries make comparison of postoperative results highly challenging. Furthermore, most studies are retrospective which further lowers the scientific value. The highest quality of medical evidence is provided by randomized controlled trials, and so far there are none available except for a small Egyptian study comparing K-wires to lateral plates of titanium (El-Saeed et al. 2019). An excellent future opportunity would be to conduct an RCT in which phalangeal fractures of a certain pattern, without injuries to the joints or surrounding soft tissues were randomized to different treatments. This would be time consuming above all, but also costly. On the other hand, it would be a welcome and much needed contribution to evidence-based treatment in hand surgery.

Adhesion barriers have been explored by hand surgeons for decades. The results have been promising in some, but few have reached the market. The problem of adhesion formation and finger stiffness persists and there is certainly a need for a remedy of some kind. Our study of Dynavisc® in fracture surgery failed to show positive results of this adhesion barrier. However, the product is marketed for nerve surgery and tendon surgery. There is evidence of effect on pain and postsurgical adhesions in spine surgery and gynaecological surgery from Oxiplex® with the same composition as Dynavisc®. So far there is however no convincing evidence of the effect of Dynavisc® in hand surgery applications, and still, it is sold and used. A well conducted study on tenolysis for instance, preferably an RCT, testing the product against placebo, would be appreciated.

The FRAP and DendroPrime materials, and further developments of these, have the potential to become suitable for many different applications in the body. The biocompatibility and fixation strength shown so far is highly promising. These materials are well-placed to undergo further development with respect to chemical composition, properties and applications. Our collaboration with KTH has already generated new ideas and spin-offs, but the road to clinical implementation is long. The next step in this process is a long-term study of the effect of the materials *in vivo* on humans. For hand surgery applications, a cadaver study for biomechanical testing in the human hand is already planned. We have shown that the ability to bond to bone and work as a fixation for fractures without disturbing bone healing or surrounding soft tissues is remarkable and it should be further explored. The ability to decrease adhesions around metal implants by coating them with the material is another unique characteristic that could be refined further and has the potential to be an important contribution in fracture fixation in hand surgery.

In this thesis the main clinical problems of fracture surgery in the fingers have been addressed. An osteosynthesis method supplying stable enough fixation for early range of motion exercises with materials not causing adhesions to soft tissue could dramatically improve finger fracture surgery in the future. We hope that our efforts and future projects have moved us a bit closer to reaching this goal.

## SUMMARY IN SWEDISH – SAMMANFATTNING PÅ SVENSKA

Fingerfrakturer är den näst vanligaste frakturen i övre extremiteten, bara handledsfrakturer är vanligare. De allra flesta fingerfrakturer kan behandlas konservativt, dvs utan operation, med gips, skena eller tejpling. Om felställningen är för stor och inte går att slutet reponera till ett acceptabelt läge, om frakturen är mycket instabil eller påverkar en led kan kirurgisk behandling bli aktuell. Den klassiska och vanligaste behandlingen då är sluten reposition och stiftfixation. Behöver man öppna huden för att reponera frakturen kan man välja mellan att stifta, skruva eller plattfixera frakturen beroende på typ av fraktur bl.a. Externfixation med en yttre ram som håller frakturbitarna på plats kan också vara ett alternativ. Oavsett operationsmetod eller gipsbehandling är det viktigt att inte hålla fingret stilla för länge. Då uppstår sammanväxningar i mjukdelarna, lederna stelnar och resultatet blir ett stelt finger.

I den här avhandlingen har olika aspekter av fingerfalangfrakturer studerats.

I den första studien tittade vi retrospektivt på de slutna, grund- och mellanfalangsfrakturer som inte engagerar lederna som behandlats kirurgiskt på handkirurgiska kliniken på Södersjukhuset 2010–2014. Journaler och röntgenbilder gick igenom, frakturer och behandlingar kategoriserades, sjukskrivningsperioder noterades, och framförallt beskrevs reoperationsfrekvens samt orsaker till reoperation. Vi fann att plattfixerade frakturer opererades om i större utsträckning än frakturer som skruvats eller stiftfixerats. Platta var också den metod som främst använts vid komplicerade flerfragmentsfrakturer. Orsaken till reoperation var till allra största delen ledstelhet pga. sammanväxningar mellan mjukdelar, ben och metall.

Resultaten från den första studien väckte frågor kring om man kunde påverka resultaten på något sätt. Plattfixation kan vara enda möjliga alternativ vid frakturer med många fragment men samtidigt ger metoden upphov till sammanväxningar som orsakar fingerstelhet. En adhesionsbarriär mellan metallen i plattan och kringliggande mjukdelar kunde vara ett alternativ. Att limma ihop en multifragmenterad fraktur kunde också möjligen vara en lösning. En kontakt med en forskargrupp på KTH som arbetade med just det senare togs, i syfte att på sikt ta fram en produkt som skulle kunna förbättra våra metoder för frakturfixation inom handkirurgin.

I studie II presenteras de första resultaten av samarbetet med KTH. Vi har aktivt deltagit i utvecklandet av FRAP-ett fiberarmerat benplåster som fäster direkt mot benytan baserat på thiol-ene-click-kemi. FRAP byggs upp i lager till ett stadigt plåster, en självhäftande platta. En primer binder konstruktionen mot benytan och sedan upp mot själva limmet. En remsa bräcknät läggs ovanpå och sedan härddas konstruktionen med högenergiljus, i detta fall med en tandläkarlampa. FRAP:en byggs sedan lager för lager, tills tillräcklig stabilitet uppnåtts och avlutas med ett lager lim för att få en slät yta. FRAP har testats av oss avseende hållfasthet i uttrötningstest i labbet på frakturerat grisfotsben och jämförts med både korsade stift och en standardplatta som används i kliniken (AO compact hand1,5). Den har också utvärderats i en frakturmodell på lårben på rått avseende effekt på benläkning, vidhäftningsförmåga, inflammation och hållfasthet efter fem veckor. FRAP visade sig vara biokompatibel, dvs påverkade inte celler eller gav upphov till mutationer. Ingen inflammation sågs runt FRAP och benläkningen påverkades inte negativt av dess närvaro. Vidhäftningsförmågan mot ben var fortsatt god efter fem veckor.

Biomekaniktesterna visar att FRAP har en styrka god nog för handrehabilitering, och ger upp till en viss belastning, nästan lika god fixering som en platta. Resultaten verkar mycket lovande för fortsatt utveckling av tekniken.

I studie III ville vi testa en på marknaden tillgänglig adhesionsbarriär, dvs ett material som ska skydda vävnader från varandra och motverka sammanväxningar. Produkten heter Dynavisc<sup>®</sup> och är en gel som saluförs för handkirurgi utan att det finns några övertygande bevis i litteraturen för att den skulle ha effekt vid handkirurgiska ingrepp. Gelen ska minska inflammation och förhindra adherensbildning enligt tillverkaren. Innehållet är carboxymethylcellulosa och polyethylenglykol. Vi testade gelen i en pilotstudie på 10 patienter mellan mars 2016 och september 2017, där gelen applicerades vid plattosteosyntes på grundfalangsfraktur eller korrektionsosteotomi på grundfalang. Utvärdering vid tre månader visade att bara två patienter nått det uppsatta målet om en rörlighet max 20° sämre än motsvarande finger på andra handen. Således fann vi inte en tydlig effekt av Dynavisc<sup>®</sup> som kunde motivera en randomiserad kontrollerad studie som varit vår ursprungliga plan.

Idén till studie IV kom när vi vid avslut av råtterna i studie II såg att inga sammanväxningar bildats runt FRAP mot omkringliggande mjukdelar efter 5 v. Tanke med denna nya studie var att testa en vidareutveckling av limmet från studie II, kallat DendroPrime, som en adherensbarriär vid plattfixation i en kaninmodell. Kaniner försågs med en platta på fotsulesidan av andra tån på baktassarna. Ena tån fick en vanlig metallplatta medan den andra tån fick en platta täckt med DendroPrime. Böjsenorna löpte över plattorna och kaninerna gick i sju veckor innan de avlivades. Sammanväxningar runt plattorna inspekterades och rörlighet i tåns ytterled mättes. Man såg mindre adherenser runt plattor täckta med DendroPrime än runt bara plattor samt en statistiskt signifikant bättre rörlighet i ytterleden vid de flesta mätpunkterna hos tår med en DendroPrime-täckt platta.

Sammanfattningsvis har denna avhandling visat att fingerstelhet efter frakturkirurgi är den vanligaste komplikationen och vanligaste orsaken till reoperation. Den har också visat att de nya material som studerats i samarbete med KTH både kan fungera som en fixationsmetod för frakturer och som en adhesionsbarriär eftersom materialet inte orsakar sammanväxningar mot omkringliggande mjukdelar. Slutligen har den visat att Dynavisc<sup>®</sup> inte verkar bidra till mindre sammanväxningar och fingerstelhet efter frakturkirurgi. Dessa resultat har givit upphov till nya forskningsfrågor och det nya materialet från studie II och studie IV testas redan i nya försök.

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## REFERENCES

2013. "World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects." *Jama* 310(20):2191-2194.
- Ashmead, D. th, D. M. Rothkopf, R. L. Walton and J. B. Jupiter. 1992. "Treatment of hand injuries by external fixation." *J Hand Surg Am* 17(5):954-964.
- Assietti, R., A. Mora and M. Brayda-Bruno. 2008. "Use of carboxymethylcellulose/polyethylene oxide gel in microdiscectomy with interlaminectomy: a case series comparison with long-term follow-up." *Spine (Phila Pa 1976)* 33(16):1762-1765.
- Ataker, Y., S. Uludag, S. C. Ece and E. Gudemez. 2017. "Early active motion after rigid internal fixation of unstable extra-articular fractures of the proximal phalanx." *J Hand Surg Eur Vol* 42(8):803-809.
- Bannasch, H., A. K. Heermann, N. Iblher, A. Momeni, J. Schulte-Mönting and G. B. Stark. 2010. "Ten years stable internal fixation of metacarpal and phalangeal hand fractures-risk factor and outcome analysis show no increase of complications in the treatment of open compared with closed fractures." *J Trauma* 68(3):624-628.
- Barrett, D. G., G. G. Bushnell and P. B. Messersmith. 2013. "Mechanically Robust, Negative-Swelling, Mussel-Inspired Tissue Adhesives." *Advanced Healthcare Materials* 2(5):745-755.
- Barton, N. J. 1984. "Fractures of the hand." *J Bone Joint Surg Br* 66(2):159-167.
- Battiston B, Berzero F, Piero DG. 2013. "Preliminary report on a new adhesion gel barrier (Dynavisc®) in hand surgery." In FESSH. Antalya, Turkey.
- Başar, H., B. Başar, O. Başçı, O. M. Topkar, B. Erol and C. Tetik. 2015. "Comparison of treatment of oblique and spiral metacarpal and phalangeal fractures with mini plate plus screw or screw only." *Arch Orthop Trauma Surg* 135(4):499-504.
- Belsky, M. R., R. G. Eaton and L. B. Lane. 1984. "Closed reduction and internal fixation of proximal phalangeal fractures." *J Hand Surg Am* 9(5):725-729.
- Bhat, Y. M., S. Banerjee, B. A. Barth, S. S. Chauhan, K. T. Gottlieb, V. Konda, J. T. Maple, F. M. Murad, P. R. Pfau, D. K. Pleskow, U. D. Siddiqui, J. L. Tokar, A. Wang and S. A. Rodriguez. 2013. "Tissue adhesives: cyanoacrylate glue and fibrin sealant." *Gastrointest Endosc* 78(2):209-215.
- Bhatt, R. A., S. Schmidt and F. Stang. 2014. "Methods and pitfalls in treatment of fractures in the digits." *Clin Plast Surg* 41(3):429-450.
- Bible, J. E. and H. R. Mir. 2015. "External Fixation: Principles and Applications." *J Am Acad Orthop Surg* 23(11):683-690.
- Black, D. M., R. J. Mann, R. M. Constance and A. U. Daniels. 1986. "The stability of internal fixation in the proximal phalanx." *J Hand Surg Am* 11(5):672-677.
- Borbas, P., M. Dreu, A. Poggetti, M. Calcagni and T. Giesen. 2016. "Treatment of proximal phalangeal fractures with an antegrade intramedullary screw: a cadaver study." *J Hand Surg Eur Vol* 41(7):683-687.
- Bosscha, K. and J. P. Snellen. 1993. "Internal fixation of metacarpal and phalangeal fractures with AO minifragment screws and plates: a prospective study." *Injury* 24(3):166-168.

- Bostman, O. and H. Pihlajamaki. 1996. "Routine implant removal after fracture surgery: a potentially reducible consumer of hospital resources in trauma units." *J Trauma* 41(5):846-849.
- Brei-Thoma, P., E. Vogelin and T. Franz. 2015. "Plate fixation of extra-articular fractures of the proximal phalanx: do new implants cause less problems?" *Arch Orthop Trauma Surg* 135(3):439-445.
- Carmona, A., J. J. Hidalgo Diaz, S. Facca, Y. Igeta, C. Pizza and P. Liverneaux. 2018. "Revision surgery in carpal tunnel syndrome: a retrospective study comparing the Canaletto(R) device alone versus a combination of Canaletto((R)) and Dynavisc((R)) gel." *Hand Surg Rehabil*.
- Carpenter, S. and R. S. Rohde. 2013. "Treatment of phalangeal fractures." *Hand Clin* 29(4):519-534.
- Chow, S. P., W. K. Pun, Y. C. So, K. D. Luk, K. Y. Chiu, K. H. Ng, C. Ng and C. Crosby. 1991. "A prospective study of 245 open digital fractures of the hand." *J Hand Surg Br* 16(2):137-140.
- Chung, K. C. and S. V. Spilson. 2001. "The frequency and epidemiology of hand and forearm fractures in the United States." *J Hand Surg Am* 26(5):908-915.
- Dabezies, E. J. and J. P. Schutte. 1986. "Fixation of metacarpal and phalangeal fractures with miniature plates and screws." *J Hand Surg Am* 11(2):283-288.
- De Jonge, J. J., J. Kingma, B. van der Lei and H. J. Klasen. 1994. "Phalangeal fractures of the hand. An analysis of gender and age-related incidence and aetiology." *J Hand Surg Br* 19(2):168-170.
- de Putter, C. E., R. W. Selles, S. Polinder, M. J. Panneman, S. E. Hovius and E. F. van Beeck. 2012. "Economic impact of hand and wrist injuries: health-care costs and productivity costs in a population-based study." *J Bone Joint Surg Am* 94(9):e56.
- del Pinal, F., E. Moraleda, J. S. Ruas, G. H. de Piero and L. Cerezal. 2015. "Minimally invasive fixation of fractures of the phalanges and metacarpals with intramedullary cannulated headless compression screws." *J Hand Surg Am* 40(4):692-700.
- Demirkan, F., N. Colakoglu, O. Herek and G. Erkula. 2002. "The use of amniotic membrane in flexor tendon repair: an experimental model." *Arch Orthop Trauma Surg* 122(7):396-399.
- Di Guiseppe P, Gregorelli C, Tunesi D. 2015. "Prevention of tendon adhesion after surgery with a new gel-formulated adhesion barrier (Dynavisc®)." In FESSH. Milan Italy 17-20 june.
- Doht, S., R. H. Meffert, M. J. Raschke, T. Blunk and S. Ochman. 2014. "Biomechanical analysis of the efficacy of locking plates during cyclic loading in metacarpal fractures." *ScientificWorldJournal* 2014:648787.
- Eberlin, K. R., A. Babushkina, J. R. Neira and C. S. Mudgal. 2014. "Outcomes of closed reduction and periarticular pinning of base and shaft fractures of the proximal phalanx." *J Hand Surg Am* 39(8):1524-1528.
- Edsfeldt, S., D. Rempel, K. Kursu, E. Diao and L. Lattanza. 2015. "In vivo flexor tendon forces generated during different rehabilitation exercises." *J Hand Surg Eur Vol* 40(7):705-710.
- Egloff, C., J. Sproedt and A. R. Jandali. 2012. "[Results after osteosynthesis of extraarticular proximal phalangeal fractures]." *Handchir Mikrochir Plast Chir* 44(1):5-10.



Ekelund, A. and O. S. Nilsson. 1991. "Tissue adhesives inhibit experimental new bone formation." *Int Orthop* 15(4):331-334.

El-Saeed, M., A. Sallam, M. Radwan and A. Metwally. 2019. "Kirschner Wires Versus Titanium Plates and Screws in Management of Unstable Phalangeal Fractures: A Randomized, Controlled Clinical Trial." *J Hand Surg Am*.

Esteban-Feliu, I., I. Gallardo-Calero, S. Barrera-Ochoa, A. Lluch-Bergada, S. Alabau-Rodriguez and X. Mir-Bullo. 2019. "Analysis of 3 Different Operative Techniques for Extra-articular Fractures of the Phalanges and Metacarpals." *Hand (N Y)*:1558944719873144.

Farrar, David F. 2012. "Bone adhesives for trauma surgery: a review of challenges and developments." *International journal of adhesion & adhesives* 33:89-97.

Faruqui, S., P. J. Stern and T. R. Kiefhaber. 2012. "Percutaneous pinning of fractures in the proximal third of the proximal phalanx: complications and outcomes." *J Hand Surg Am* 37(7):1342-1348.

Feehan, L. M. 2003. "Early controlled mobilization of potentially unstable extra-articular hand fractures." *J Hand Ther* 16(2):161-170.

Franz, T., U. von Wartburg, S. Schibli-Beer, F. J. Jung, A. R. Jandali, M. Calcagni and U. Hug. 2012. "Extra-articular fractures of the proximal phalanges of the fingers: a comparison of 2 methods of functional, conservative treatment." *J Hand Surg Am* 37(5):889-898.

Freeland, A. E., M. A. Hardy and S. Singletary. 2003. "Rehabilitation for proximal phalangeal fractures." *J Hand Ther* 16(2):129-142.

Freeland, A. E., V. Sud and S. G. Lindley. 2001. "Unilateral intrinsic resection of the lateral band and oblique fibers of the metacarpophalangeal joint for proximal phalangeal fracture." *Tech Hand Up Extrem Surg* 5(2):85-90.

Frykman, E., S. Jacobsson and B. Widenfalk. 1993. "Fibrin sealant in prevention of flexor tendon adhesions: an experimental study in the rabbit." *J Hand Surg Am* 18(1):68-75.

Fuchs, N., N. Smorgick, I. Ben Ami, Z. Vaknin, Y. Tovbin, R. Halperin and M. Pansky. 2014. "Intercoat (Oxiplex/AP gel) for preventing intrauterine adhesions after operative hysteroscopy for suspected retained products of conception: double-blind, prospective, randomized pilot study." *J Minim Invasive Gynecol* 21(1):126-130.

Fyfe, I. S. and S. Mason. 1979. "The mechanical stability of internal fixation of fractured phalanges." *Hand* 11(1):50-54.

Giddins, G. E. 2015. "The non-operative management of hand fractures." *J Hand Surg Eur Vol* 40(1):33-41.

Giesen, T., R. Gazzola, A. Poggetti, P. Giovanoli and M. Calcagni. 2016. "Intramedullary headless screw fixation for fractures of the proximal and middle phalanges in the digits of the hand: a review of 31 consecutive fractures." *J Hand Surg Eur Vol* 41(7):688-694.

Golash, A., A. Kay, J. G. Warner, F. Peck, J. S. Watson and V. C. Lees. 2003. "Efficacy of ADCON-T/N after primary flexor tendon repair in Zone II: a controlled clinical trial." *J Hand Surg Br* 28(2):113-115.

Gould, W. L., R. J. Belsole and W. H. Skelton, Jr. 1984. "Tension-band stabilization of transverse fractures: an experimental analysis." *Plast Reconstr Surg* 73(1):111-116.

- Guerrero, E. M., R. E. Baumgartner, A. E. Federer, S. K. Mithani, D. S. Ruch and M. J. Richard. 2019. "Complications of Low-Profile Plate Fixation of Phalanx Fractures." *Hand (N Y)*:1558944719855684.
- Guimberteau, J. C., J. P. Delage, D. A. McGrouther and J. K. Wong. 2010. "The microvacuolar system: how connective tissue sliding works." *J Hand Surg Eur Vol* 35(8):614-622.
- Hagberg, L. and B. Gerdin. 1992. "Sodium hyaluronate as an adjunct in adhesion prevention after flexor tendon surgery in rabbits." *J Hand Surg Am* 17(5):935-941.
- Hakansson, J., M. Mahlapuu, L. Ekstrom, K. Olmarker and M. Wiig. 2012. "Effect of lactoferrin peptide (PXL01) on rabbit digit mobility after flexor tendon repair." *J Hand Surg Am* 37(12):2519-2525.
- HAKIR. 2014. "HAKIR årsrapport 2014."
- Hanff, G. and L. Hagberg. 1998. "Prevention of restrictive adhesions with expanded polytetrafluoroethylene diffusible membrane following flexor tendon repair: an experimental study in rabbits." *J Hand Surg Am* 23(4):658-664.
- Hed Y, Öberg K, Berg S, Nordberg A, von Holst H, Malkoch M. 2013. "Multipurpose heterofunctional dendritic scaffolds as crosslinkers towards functional soft hydrogels and implant adhesives in bone fracture applications." *Journal of Materials Chemistry B*; 2013(44):6015-6019.
- Held, M., P. Jordaán, M. Laubscher, M. Singer and M. Solomons. 2013. "Conservative treatment of fractures of the proximal phalanx: an option even for unstable fracture patterns." *Hand Surg* 18(2):229-234.
- Henry, M. H. 2008. "Fractures of the proximal phalanx and metacarpals in the hand: preferred methods of stabilization." *J Am Acad Orthop Surg* 16(10):586-595.
- Hove, L. M. 1993. "Fractures of the hand. Distribution and relative incidence." *Scand J Plast Reconstr Surg Hand Surg* 27(4):317-319.
- Hsu, L. P., E. G. Schwartz, D. M. Kalainov, F. Chen and R. L. Makowiec. 2011. "Complications of K-wire fixation in procedures involving the hand and wrist." *J Hand Surg Am* 36(4):610-616.
- Huffaker, W. H., R. C. Wray, Jr. and P. M. Weeks. 1979. "Factors influencing final range of motion in the fingers after fractures of the hand." *Plast Reconstr Surg* 63(1):82-87.
- Ibanez, D. S., F. L. Rodrigues, R. S. Salviani, F. A. Roberto, J. R. Pengo Junior and M. A. Aita. 2015. "Experimental trial on surgical treatment for transverse fractures of the proximal phalanx: technique using intramedullary conical compression screw versus lateral compression plate." *Rev Bras Ortop* 50(5):509-514.
- Ikemura, K. and T. Endo. 2010. "A review of our development of dental adhesives--effects of radical polymerization initiators and adhesive monomers on adhesion." *Dent Mater J* 29(2):109-121.
- James, J. I. 1970. "The assessment and management of the injured hand." *Hand* 2(2):97-105.
- Jensen, M. P., P. Karoly and S. Braver. 1986. "The measurement of clinical pain intensity: a comparison of six methods." *Pain* 27(1):117-126.

- Jones, M. E., S. Burnett, A. Southgate, P. Sibbons, A. O. Grobbelaar and C. J. Green. 2002. "The role of human-derived fibrin sealant in the reduction of postoperative flexor tendon adhesion formation in rabbits." *J Hand Surg Br* 27(3):278-282.
- Jovanovic, N., E. Aldlyami, B. Saraj, M. Fm Seidam, H. Badawi, A. Shaat, K. Alawadi and C. Dodakundi. 2018. "Intramedullary Percutaneous Fixation of Extra-Articular Proximal and Middle Phalanx Fractures." *Tech Hand Up Extrem Surg* 22(2):51-56.
- Kappos, E. A., P. Esenwein, M. Meoli, R. Meier and J. Grunert. 2015. "Implantation of a denaturated cellulose adhesion barrier after plate osteosynthesis of finger proximal phalangeal fractures: results of a randomized controlled trial." *J Hand Surg Eur Vol*.
- Karl, J. W., P. R. Olson and M. P. Rosenwasser. 2015. "The Epidemiology of Upper Extremity Fractures in the United States, 2009." *J Orthop Trauma* 29(8):e242-244.
- Kim, B. J., D. X. Oh, S. Kim, J. H. Seo, D. S. Hwang, A. Masic, D. K. Han and H. J. Cha. 2014. "Mussel-mimetic protein-based adhesive hydrogel." *Biomacromolecules* 15(5):1579-1585.
- Kootstra, T. J. M., J. Keizer, A. Bhashyam, R. M. Houwert, E. M. M. Verleisdonk, M. van Heijl and D. van der Velde. 2019. "Patient-Reported Outcomes and Complications After Surgical Fixation of 143 Proximal Phalanx Fractures." *J Hand Surg Am*.
- Kose, A., M. Topal, M. C. Engin, A. Sencan, R. Dincer and T. Baran. 2018. "Comparison of low-profile plate-screw and Kirschner-wire osteosynthesis outcomes in extra-articular unstable proximal phalangeal fractures." *Eur J Orthop Surg Traumatol*.
- Kozin, S. H., J. J. Thoder and G. Lieberman. 2000. "Operative treatment of metacarpal and phalangeal shaft fractures." *J Am Acad Orthop Surg* 8(2):111-121.
- Kuczynski, K. 1968. "The proximal interphalangeal joint. Anatomy and causes of stiffness in the fingers." *J Bone Joint Surg Br* 50(3):656-663.
- Kurzen, P., C. Fusetti, M. Bonaccio and L. Nagy. 2006. "Complications after plate fixation of phalangeal fractures." *J Trauma* 60(4):841-843.
- LaStayo, P. C., K. M. Winters and M. Hardy. 2003. "Fracture healing: bone healing, fracture management, and current concepts related to the hand." *J Hand Ther* 16(2):81-93.
- Lees, V. C. 2016. "Commentary on Implantation of a denatured cellulose adhesion barrier after plate osteosynthesis of finger proximal phalangeal fractures: results of a randomized controlled trial. E. A. Kappos, P. Esenwein, M. Meoli, R. Meier and J. Grunert. *J Hand Surg Eur*. 2016, 41: 413-20." *J Hand Surg Eur Vol* 41(4):421-422.
- Lees, V. C., D. Warwick, P. Gillespie, A. Brown, M. Akhavan, D. Dewar, D. Boyce, S. Papanastasiou, R. Ragoowansi and J. Wong. 2015. "A multicentre, randomized, double-blind trial of the safety and efficacy of mannose-6-phosphate in patients having Zone II flexor tendon repairs." *J Hand Surg Eur Vol* 40(7):682-694.
- Lei, W., R. J. Ehmsen, R. P. Chiacchierini, J. L. Krelle and G. S. Dizerega. 2013. "Reduction of Leg Pain by Oxiplex® Gel After Lumbar Discectomy in Patients with Predominant Leg Pain and Elevated Levels of Lower Back Pain: A Prospective, Randomized, Blinded, Multi-Center Clinical Study." *J Spinal Disord Tech*.
- Liodaki, E., T. Kisch, E. Wenzel, P. Mailander and F. Stang. 2017. "Percutaneous Cannulated Compression Screw Osteosynthesis in Phalanx Fractures: The Surgical Technique, the Indications, and the Results." *Eplasty* 17:e8.

- Loiselle, A. E., M. Kelly and W. C. Hammert. 2016. "Biological Augmentation of Flexor Tendon Repair: A Challenging Cellular Landscape." *J Hand Surg Am* 41(1):144-149; quiz 149.
- Lucchina, S., F. Maggiulli, P. Tos, M. Ionac and C. Fusetti. 2015. "Can an adipofascial flap be used to prevent adhesions after plating of the proximal phalanx? A case report." *Chir Main* 34(2):86-90.
- Markiewitz, A. D. 2013. "Complications of hand fractures and their prevention." *Hand Clin* 29(4):601-620.
- Massengill, J. B., H. Alexander, N. Langrana and A. Mylod. 1982. "A phalangeal fracture model--quantitative analysis of rigidity and failure." *J Hand Surg Am* 7(3):264-270.
- Massengill, J. B., H. Alexander, J. R. Parson and M. J. Schechter. 1979. "Mechanical analysis of Kirschner wire fixation in a phalangeal model." *J Hand Surg Am* 4(4):351-356.
- Mathiowetz, V., K. Weber, G. Volland and N. Kashman. 1984. "Reliability and validity of grip and pinch strength evaluations." *J Hand Surg Am* 9(2):222-226.
- Miller, L., L. Ada, J. Crosbie and A. Wajon. 2017. "Pattern of recovery after open reduction and internal fixation of proximal phalangeal fractures in the finger: a prospective longitudinal study." *J Hand Surg Eur Vol* 42(2):137-143.
- Miller, L., J. Crosbie, A. Wajon and L. Ada. 2016. "No difference between two types of exercise after proximal phalangeal fracture fixation: a randomised trial." *J Physiother* 62(1):12-19.
- Namba, J., K. Shimada, M. Saito, T. Murase, H. Yamada and H. Yoshikawa. 2007. "Modulation of peritendinous adhesion formation by alginate solution in a rabbit flexor tendon model." *J Biomed Mater Res B Appl Biomater* 80(1):273-279.
- Nazzal, A., S. Lozano-Calderon, J. B. Jupiter, J. S. Rosenzweig, M. A. Randolph and S. G. Lee. 2006. "A histologic analysis of the effects of stainless steel and titanium implants adjacent to tendons: an experimental rabbit study." *J Hand Surg Am* 31(7):1123-1130.
- Nordberg, A., P. Antoni, M. I. Montanez, A. Hult, H. Von Holst and M. Malkoch. 2010. "Highly adhesive phenolic compounds as interfacial primers for bone fracture fixations." *ACS Appl Mater Interfaces* 2(3):654-657.
- Nordberg, A., H. von Holst, K. Brolin and A. Beckman. 2007. "Vertebral fractures fixation with composite patch fibre reinforced adhesives." *Biomed Mater Eng* 17(5):299-308.
- Nunley, J. A. and P. Kloen. 1991. "Biomechanical and functional testing of plate fixation devices for proximal phalangeal fractures." *J Hand Surg Am* 16(6):991-998.
- Oei, T. S., P. J. Kloppe, J. A. Spaas and P. Buma. 1996. "Reconstruction of the flexor tendon sheath. An experimental study in rabbits." *J Hand Surg Br* 21(1):72-83.
- Olmarker, K., L. Ekstrom, J. Hakansson, E. Nilsson, M. Wiig and M. Mahlapuu. 2010. "Model for assessment of mobility of toes and healing of tendons in rabbits." *J Plast Surg Hand Surg* 44(6):266-271.
- Onishi, T., S. Omokawa, T. Shimizu, R. Fujitani, K. Shigematsu and Y. Tanaka. 2015. "Predictors of Postoperative Finger Stiffness in Unstable Proximal Phalangeal Fractures." *Plast Reconstr Surg Glob Open* 3(6):e431.

Ouellette, E. A., J. J. Dennis, L. L. Latta, E. L. Milne and A. L. Makowski. 2004. "The role of soft tissues in plate fixation of proximal phalanx fractures." *Clin Orthop Relat Res*(418):213-218.

Page, S. M. and P. J. Stern. 1998. "Complications and range of motion following plate fixation of metacarpal and phalangeal fractures." *J Hand Surg Am* 23(5):827-832.

Pandey, R., N. Soni, H. Bhayana, R. Malhotra, A. Pankaj and S. S. Arora. 2018. "Hand function outcome in closed small bone fractures treated by open reduction and internal fixation by mini plate or closed crossed pinning: a randomized controlled trail." *Musculoskelet Surg*.

Peterson, W. W., P. R. Manske, J. Dunlap, D. S. Horwitz and B. Kahn. 1990. "Effect of various methods of restoring flexor sheath integrity on the formation of adhesions after tendon injury." *J Hand Surg Am* 15(1):48-56.

Pinkerton, M. C. 1942. "Amnioplastin for adherent digital flexor tendons." ed. Edin. *The Lancet*.

Pratt, D. R. 1959. "Exposing fractures of the proximal phalanx of the finger longitudinally through the dorsal extensor apparatus." *Clin Orthop* 15:22-26.

Pun, W. K., S. P. Chow, Y. C. So, K. D. Luk, F. K. Ip, K. C. Chan, W. K. Ngai, C. Crosby and C. Ng. 1989. "A prospective study on 284 digital fractures of the hand." *J Hand Surg Am* 14(3):474-481.

Pun, W. K., S. P. Chow, Y. C. So, K. D. Luk, W. K. Ngai, F. K. Ip, W. H. Peng, C. Ng and C. Crosby. 1991. "Unstable phalangeal fractures: treatment by A.O. screw and plate fixation." *J Hand Surg Am* 16(1):113-117.

Reformat, D. D., G. G. Nores, G. Lam, D. Cuzzzone, J. B. Hill, H. Muresan and V. Thanik. 2018. "Outcome Analysis of Metacarpal and Phalangeal Fixation Techniques at Bellevue Hospital." *Ann Plast Surg* 81(4):407-410.

Reith, G., V. Schmitz-Greven, K. O. Hensel, M. M. Schneider, T. Tinschmann, B. Bouillon and C. Probst. 2015. "Metal implant removal: benefits and drawbacks--a patient survey." *BMC Surg* 15:96.

Rex, C., R. Vignesh, M. Javed, S. C. Balaji, C. Premanand and S. A. Zakki. 2015. "Safe corridors for K-wiring in phalangeal fractures." *Indian J Orthop* 49(4):388-392.

Riccio, M. "Prevention of peritendinous adhesions after tenolysis by means of a carbomethylcellulose (CMC), poly-ethylene oxide (PEO) based gel: a light microscope study in the rabbit." Manuscript <https://www.fziomed.com/technology/reference-library>.

Robinson, L. P., M. P. Gaspar, A. B. Strohl, S. L. Teplitsky, S. D. Gandhi, P. M. Kane and A. L. Osterman. 2017. "Dorsal versus lateral plate fixation of finger proximal phalangeal fractures: a retrospective study." *Arch Orthop Trauma Surg* 137(4):567-572.

Rosberg, H. E., K. S. Carlsson and L. B. Dahlin. 2005. "Prospective study of patients with injuries to the hand and forearm: costs, function, and general health." *Scand J Plast Reconstr Surg Hand Surg* 39(6):360-369.

Rosberg, H. E. and L. B. Dahlin. 2004. "Epidemiology of hand injuries in a middle-sized city in southern Sweden: a retrospective comparison of 1989 and 1997." *Scand J Plast Reconstr Surg Hand Surg* 38(6):347-355.

- Saied, A. R. and M. Sabet Jahromi. 2018. "Treatment of proximal phalanx fractures: transarticular pinning the metacarpophalangeal joint or cross pinning from the base of the proximal phalanx-a prospective study." *Eur J Trauma Emerg Surg*.
- Schadel-Hopfner, M., J. Windolf, G. Antes, S. Sauerland and M. K. Diener. 2008. "Evidence-based hand surgery: the role of Cochrane reviews." *J Hand Surg Eur Vol* 33(2):110-117.
- Scognamiglio, F., A. Travan, I. Rustighi, P. Tarchi, S. Palmisano, E. Marsich, M. Borgogna, I. Donati, N. de Manzini and S. Paoletti. 2016. "Adhesive and sealant interfaces for general surgery applications." *J Biomed Mater Res B Appl Biomater* 104(3):626-639.
- Serrano, F. J. C., L. M. Pinzon, D. M. Narvaez, C. I. C. Paez, C. L. Moreno-Serrano, D. M. Tabima, F. Salcedo, J. C. Briceno and J. P. Casas-Rodriguez. 2017. "Evaluation of a water-resistant and biocompatible adhesive with potential use in bone fractures." *Journal of Adhesion Science and Technology* 31(13):1480-1495.
- Shanmugam, R., M. Ernst, K. Stoffel, M. F. Fischer, D. Wahl, R. G. Richards and B. Gueorguiev. 2015. "Angular stable lateral plating is a valid alternative to conventional plate fixation in the proximal phalanx. A biomechanical study." *Clin Biomech (Bristol, Avon)*.
- Shewring, D. J., R. W. Trickett and A. Smith. 2018. "Fractures at the junction of diaphysis and metaphysis of the proximal phalanges in adults." *J Hand Surg Eur Vol* 43(5):506-512.
- Sierra, David and Renato Salz. 1996. *Surgical adhesives and sealants Current technology and Applications*. Lancaster, Pennsylvania: Technomic publishing company, inc.
- Singh, J., K. Jain, Mruthyunjaya and R. Ravishankar. 2011. "Outcome of closed proximal phalangeal fractures of the hand." *Indian J Orthop* 45(5):432-438.
- Spotnitz, W. D. 2010. "Fibrin sealant: past, present, and future: a brief review." *World J Surg* 34(4):632-634.
- Sraj, S. 2016. "A Simple Phalangeal External Fixator Using Kirschner Wires and Locking Balls: No Need for Cement or Rubber Bands." *J Hand Surg Am* 41(7):e217-221.
- Stern, P. J., M. J. Wieser and D. G. Reilly. 1987. "Complications of plate fixation in the hand skeleton." *Clin Orthop Relat Res*(214):59-65.
- Strauch, B., W. de Moura, M. Ferder, C. Hall, A. Sagi and B. Greenstein. 1985. "The fate of tendon healing after restoration of the integrity of the tendon sheath with autogenous vein grafts." *J Hand Surg Am* 10(6 Pt 1):790-795.
- Sungur, N., A. Uysal, U. Kocer, O. Karaaslan, M. Gumus, L. K. Sokmensuer and C. Sokmensuer. 2006. "Prevention of tendon adhesions by the reconstruction of the tendon sheath with solvent dehydrated bovine pericard: An experimental study." *J Trauma* 61(6):1467-1472.
- Takigami, H., H. Sakano and T. Saito. 2010. "Internal fixation with the low profile plate system compared with Kirschner wire fixation: clinical results of treatment for metacarpal and phalangeal fractures." *Hand Surg* 15(1):1-6.
- Thomas, B. P., R. Sreekanth and S. C. Pallapati. 2015. "Open proximal phalangeal shaft fractures of the hand treated by theta fixation." *Indian J Orthop* 49(3):312-316.
- Vaishya, R., M. Chauhan and A. Vaish. 2013. "Bone cement." *J Clin Orthop Trauma* 4(4):157-163.
- van Onselen, E. B., R. B. Karim, J. J. Hage and M. J. Ritt. 2003. "Prevalence and distribution of hand fractures." *J Hand Surg Br* 28(5):491-495.

Vanik, R. K., R. C. Weber, H. S. Matloub, J. R. Sanger and R. P. Gingrass. 1984. "The comparative strengths of internal fixation techniques." *J Hand Surg Am* 9(2):216-221.

Walter, F. L. and R. F. Papandrea. 2011. "A mini external fixator for hand and finger fractures constructed from readily available materials." *Tech Hand Up Extrem Surg* 15(4):215-218.

Wheeldon, T. 1939. "The use of cellophane as a permanent tendon sheet." *Journal of bone and joint surgery*.

Wiig, M. E., L. B. Dahlin, J. Friden, L. Hagberg, S. E. Larsen, K. Wiklund and M. Mahlapuu. 2014. "PXL01 in sodium hyaluronate for improvement of hand recovery after flexor tendon repair surgery: randomized controlled trial." *PLoS One* 9(10):e110735.

Wiig, M., K. Olmarker, J. Hakansson, L. Ekstrom, E. Nilsson and M. Mahlapuu. 2011. "A lactoferrin-derived peptide (PXL01) for the reduction of adhesion formation in flexor tendon surgery: an experimental study in rabbits." *J Hand Surg Eur Vol* 36(8):656-662.

Wright, T. A. 1968. "Early mobilization in fractures of the metacarpals and phalanges." *Can J Surg* 11(4):491-498.

Yang, T. H., S. C. Lu, W. J. Lin, K. Zhao, C. Zhao, K. N. An, I. M. Jou, P. Y. Lee, L. C. Kuo and F. C. Su. 2016. "Assessing Finger Joint Biomechanics by Applying Equal Force to Flexor Tendons In Vitro Using a Novel Simultaneous Approach." *PLoS One* 11(8):e0160301.

Zelken, J. A., A. G. Hayes, B. G. Parks, A. Al Muhit and K. R. Means, Jr. 2015. "Two versus 3 lag screws for fixation of long oblique proximal phalanx fractures of the fingers: a cadaver study." *J Hand Surg Am* 40(6):1124-1129.

Zhang, X., X. Shao, Z. Zhang, G. Zhang, Y. Yu, L. Wang and L. Lyu. 2017. "Cemented K-wire fixation for the treatment of shaft fractures of middle phalanges." *Injury*.